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THE SURGICAL CLINICS OF NORTH AMERICA

Volume 7

No. 1

CONTRIBUTION BY W. SAMPSON HANDLEY,
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THE ORIGIN OF BONE-DEPOSITS IN BREAST CANCER

How do carcinoma cells reach a bone and give rise to secondary deposits within it?

Until the recent work of Dr. J. B. Carnett this question has remained in the position in which I left it in 1904. My conclusions were based upon the necropsies of 329 cases of breast cancer which died in the Middlesex Hospital in the years 1892-1901. Among these there were 73 cases in which the bones were attacked.

I drew pointed attention to the unavoidable incompleteness of the examination of the skeleton in these cases, but I nevertheless considered that they afforded clear evidence that "bone deposits are usually secondary results of far-extending growth of cancer along the deep fascial lymphatic plexus." This is how subcutaneous nodules certainly arise, and it appeared significant that both as regards the skin and the bones the distal halves of the limbs are very rarely the seat of secondary deposits. It appeared too from the records that the femur and the humerus are especially liable to attack at the areas nearest the trunk at which they become subcutaneous and where they are, therefore, in intimate relation with the deep fascia. These areas of course are

¹This contribution was delivered as a lecture at Philadelphia General Hospital.

the great trochanter and the deltoid insertion. It is at or about these points that spontaneous fractures usually occur. Two observations seemed to me to make it very difficult to accept the current view that bone deposits arose by embolism of cancerous particles in the blood vessels.

A. The great infrequency of bone deposits distal to the knee and the elbow though non cancerous emboli are known to lodge with special frequency in the distal portions of the limbs.

B. Among 8 cases of unilateral fracture of the femur secondary to breast cancer in 6 cases the fracture was found on the same side as the primary growth.

It is so far as is known a matter of pure chance whether a cancer particle in the abdominal aorta shall pass down the right or the left iliac artery. Why is it then that advanced secondary cancer of the femur (as indicated by fracture) is three times more common on the side of the growth than upon the opposite side?

At this point I must give some account of Dr Piney's views and researches on secondary bone cancer. His excellent work on this and other subjects is one of the few bright spots in the outlook for the science of morbid histology in England. Morbid anatomy and especially its microscopic branch is at present an unfashionable branch of pathology partly because pathology presents many newer fields of enhancing interest and partly on account of the mistaken view that morbid histology is a closed and exhausted branch of knowledge.

Dr Piney was the first to trace the changes in the bone marrow as life advances. At birth all the bones except those of the cranium contain red marrow.

At puberty fat begins to replace red marrow in the diaphyses of the long bones and this conversion is more rapid in the distal than in the proximal long bones. Throughout life a patch of red marrow persists in the upper end of the humerus and the femur. The small bones of the hand and foot lose their red marrow even earlier than those of the leg and forearm. The vertebræ, sternum ossa innominata and ribs retain their red marrow in adult life.

Dr Piney states that secondary growth in bone only occurs

in red marrow. Dr. Piney could demonstrate no lymphatic vessels in the bone-marrow, though they could be easily injected in the periosteum. He found that the cancer cells in the marrow were growing in the blood-channels. The distal bones of the limbs were free from deposit, and this is explained by their containing only yellow marrow. He did not find permeation of the periosteal lymphatics. The point of emergence of the tumor on the surface of the bone corresponded to the places of exit of the veins. Upon this evidence he concluded that bone-deposits in the marrow were spread embolically in the blood-stream, explaining the immunity of the distal bones by the absence of red marrow from them which renders them an unsuitable nidus for the emboli which reach them.

Let me say here that I have never made any microscopic research on the spread of carcinoma in bone, and I accept Dr. Piney's conclusion that the disease spreads by the rich network of small blood-vessels found in it. I was concerned with a different problem, namely, how the carcinoma cells reach the bone. Centrifugal permeation of the fascial lymphatic plexus must be taken as proved, and this process must carry cancer cells to the periosteal lymphatics at the subcutaneous areas where the fascia is attached directly to the bone. Since lymphatics and veins always run together, infiltration of the wall of the comitant vein is a likely event, and subsequent extension in the bone may take place, as Piney has shown, along the blood-channels. But Dr. Piney has not adduced any evidence that the cancer cells in the first instance reach the bone by the blood-stream. We are thus faced by two plausible hypotheses of the origin of bone-deposits. Are they due to blood-embolism or to lymphatic permeation? If to the former, it should make no difference to the chances of a deposit in say the right femur, whether the primary growth is situated in the right or the left breast. Pure chance will determine whether an embolus shooting down the abdominal aorta takes the right or the left common iliac artery, and reaches the right or the left limb. Why is it then that in 8 cases showing unilateral fracture of the femur the fracture was on the same side as the primary growth in 6 cases and on the opposite side in only

2 cases? I ask Dr Piney to explain this preference for the homo lateral femur and until he can do so I shall continue to believe that cancer cells reach the bone by lymphatic permeation necessarily therefore as a rule reaching the femur on the same side as the primary growth before they reach the opposite femur

Dr Carnett's studies on secondary carcinoma in the bones carried out with the aid of modern x ray equipment and with complete radiologic examination of the entire skeleton have led him to reject the idea that bone deposits as a rule are disseminated by the blood stream. He agrees with me in believing that they result from lymphatic permeation. His conclusions however differ from my own in certain important respects and not only in regard to bone deposits but more generally as to the dissemination of cancer within the pleural and peritoneal cavities. This question has a bearing on bone deposits and must therefore be discussed.

I had laid the principal stress on the importance as a cause of visceral deposits of the implantation upon the serous surfaces of cancer particles which had reached the serous cavities. Carnett on the contrary thinks lymphatic permeation in the lymphatic chains and plexuses in and around these cavities is the more important process. The difference of view is perhaps partly an unreal one for though I still maintain that most early deposits in the pleura or peritoneum depend on the access of the cancer particles to the serous cavities it is obvious that cancer nodules cannot long exist upon the surface of a serous membrane without giving rise to wide-spread permeation of the surrounding lymphatic vessels. As I stated (Handley Cancer of the Breast 2d ed. p. 117) the occurrence of permeation and of embolic gland invasion from each of the foci thus arising (i. e. by implantation on the serosa) soon terminates the patient's existence.

In part however the difference of view is a real and important one. Dr Carnett has observed in cases of secondary deposit in the pelvic bones and the femur that chains of infected glands can often be traced right through the abdomen from the diaphragm along the aorta and its branches to the groin. He observes that this retrograde permeation of the trunk lymphatics is a more

rapid process than permeation of the small lymphatics of the fascial plexus. He has only once seen subcutaneous nodules associated with deposits in the femur. He finds that associated deposits in the lumbar vertebrae often accompany femoral and pelvic deposits, and he concludes from all these facts that the route of invasion is an intra abdominal and not a parietal one.

These observations are I think convincing and I accept Carnett's conclusions as an important addition to our knowledge of dissemination though I have no doubt that in exceptional cases cancer cells may reach the femur by the fascial route.

Carnett has further shown by the x ray method that cancer of the femur may begin in the head and neck, an occurrence very difficult to explain on the hypothesis of fascial spread.

In regard to invasion of the humerus also in opposition to my own view that invasion usually occurred from the fascia at the deltoid insertion, Carnett has put forward indubitable x ray evidence that the bone is often first attacked in the region of its head. He thinks it probable that the bone is reached by permeation along the tributaries of the infected axillary glands, a process which must occur in a relatively early stage of cancer. Moreover "the majority of the skiagrams taken during or shortly after this early stage of humeral metastasis also show early invasion of the glenoid and acromion processes of the scapula. Usually but at a somewhat later stage, the skiagrams will reveal metastasis to the outer end of the clavicle."

Here for the first time there is traced a picture of the succession of events in the invasion of the bones about the shoulder. These careful observations strongly support Dr. Carnett's conclusions, and on this subject I unreservedly accept them as correcting my own.

It is significant that in his work on bone deposits Professor Carnett has followed the method of intensive study of a small group of particular cases. Upon each of these cases a vast amount of work has been lavished in order to make the record of that case as complete as possible. He has thus obtained definite indications of the truth which could not have been elicited by any more perfunctory method.

The multiplication of imperfect case records does not help. One case well observed is worth a bushel of statistics.

One interesting fact remains to be referred to. Prof. Carnett has shown that the freedom of the distal bones of the limbs from secondary deposit to which I drew attention in 1904 is a relative freedom only and that in very late cases incipient deposits of carcinoma can be detected in the bones below the knee and below the elbow. This observation made possible by recent improvements in x ray technic is of great interest.

CLINIC OF DR JOHN BERTON CARNETT

RADIOLOGIC DEPARTMENT, PHILADELPHIA GENERAL HOSPITAL

SCIRRHOUS CARCINOMA OF BREAST WITH EXTENSIVE METASTASES

THE next patient is a colored, married woman, thirty nine years of age. She had typhoid fever in 1910 followed in a few months by an eighth month premature labor.

In the summer of 1920 she first noted a small hard lump in the right breast above the nipple. One year later, in August, 1921 her right breast was amputated for adenocarcinoma at the Woman's Hospital in New York City. At that time it was found that she had bilateral pyosalpinx. In September, 1923 bilateral salpingo oophorectomy and myomectomy were performed at St. Luke's Hospital in New York City. She reported to the surgical clinic of the latter hospital from time to time and a skiagram taken there on April 4, 1924 demonstrated "Much degenerative change, apparently metastatic, involving the os innominatum on the right side. Here and there localized rarefaction is seen elsewhere in the pelvic bones, but the appearance of these discrete areas is not so characteristic."

In late September, 1925 she developed sore throat and cough with severe pains over both sides of chest front and back. One week later on October 3, 1925 she was admitted to my service in the Radiologic Department of the Philadelphia General Hospital. At that time nothing could be found in the superficial tissues that was in any way suspicious of cancer, and the only external evidence of cancer she now exhibits are two pea sized subcutaneous nodules on the abdomen.

Both of her pectoral muscles were removed at operation. It is astonishing how little inconvenience for the ordinary affairs of life is caused by the loss of these large muscles. Within the

past few days Dr Josiah C McCracken of Shanghai China told me of the curious experience the removal of these two muscles caused one of his operated patients. In attempting to swim on her back she had so much loss of power in the affected arm that she was able to swim only in a circle.

2 Ray pictures taken of our patient during the first week after her admission revealed carcinomatous metastases of the skull the fifth sixth and seventh cervical vertebrae inner third of right clavicle both scapulae both humeri the majority of the ribs the lumbar vertebrae also the bones of the pelvis and upper third of both femora.

Bone metastases to the extent just described are not infrequent in our cases of late breast cancer. Ordinarily the disease kills the patient at this stage and only exceptional cases of whom this patient is one continue to live sufficiently longer for the disease to spread further afield in the osseous system.

In our first few cases of breast cancer with wide spread bone metastases the patients had received heavy and prolonged radiation over the chest before they came under our observation. We were inclined to believe that the radiation by keeping the disease under control within the chest had prolonged the lives of the patients thereby permitting the peripheral disease to spread much further afield before death occurred. That theory however does not apply to the patient now before you because she had not received any radiation prior to her admission.

On November 16th further skiagrams disclosed involvement of the manubrium and gladiolus. x Ray pictures taken May 1 1926 demonstrated progression of the disease in the bones previously involved with extension to left clavicle to upper ends of both radii to every vertebrae to entire femora and to right upper tibia. The left upper tibia was somewhat suspicious of early invasion.

All the vertebrae the entire pelvis both femora and both humeri exhibited profound osteoporosis in these skiagrams taken on May 1st. There has been so much absorption of lime salts that the outlines of the vertebrae are barely visible. The bodies of so many vertebrae have crumpled up that there has been a

very marked decrease in the length of the patient's torso, but this has not been accompanied by any evidence of pressure on the spinal cord. The triangular compression of numerous vertebral bodies and absorption of intervertebral disks have resulted, posteriorly, in an extensive kyphosis and anteriorly in a bulging, with convexity forward, of the sternum and the formation of

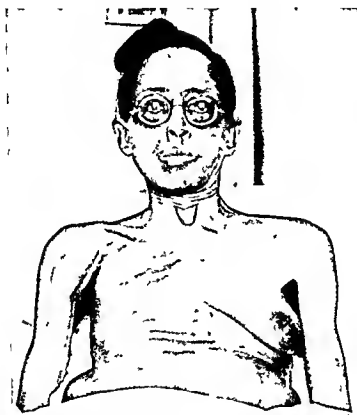


Fig 1—Foreshortening of chest. Bulging of sternum. Transverse grooves across upper abdomen.

two deep transverse furrows in the upper abdomen (Fig 1). These changes have shortened the length of the patient's torso and greatly diminished the chest capacity. Dyspnea is so marked that the patient is unable to lie flat in bed.

The May, 1926 skiagrams demonstrated such extensive bone destruction in both humeri and both femora that the nurses carried out their ministrations in daily fear of pathologic frac-

tures Within the following three months spontaneous fracture occurred in the shaft of each of these four major bones One humerus was broken when the patient rested her weight on her elbow One femur gave way when the patient tried to rotate her foot inward against the weight of the bed clothes No definite strain could be ascertained as a cause of the fracture in the other femur and humerus You will observe that all four fractures have united as demonstrated (1) by the patient's



Fig 2 —Multiple lesions in skull May 1926

ability to raise each arm and leg from the bed and (2) by the callus around each fracture shown by these skiagrams taken in late September 1926

Within the past few days these two small subcutaneous nodules have made their appearance on the abdomen I wish particularly to call your attention to the very marked enlargement and hardness of the lymph nodes in both saphenous regions and to a lesser extent in both inguinal regions I shall have

occasion later on to refer to these nodes. This edema, affecting the entire length of both lower extremities, is probably due to obstruction of venous and lymphatic return flow caused by metastatic enlargement of the deep inguinal or the lumbar lymphatic nodes. The liver is somewhat enlarged, but no nodules are palpable.

You will notice how she winces as I make moderately firm pressure over the abdomen. One of her major complaints is pain over the chest and abdomen, particularly on the left side. On gentle pressure over her relaxed abdominal muscles my



Fig 3—Metastases present in every bone in skagram

fingers dip fairly deeply without producing pain, but slightly firmer, deeper pressure *causes distress*. *Tenderness*, which is first elicited after such deep indentation of the anterior belly wall, is usually regarded as being indicative of an intra-abdominal or other deep-seated lesion. Even under such circumstances, however, it is surprising how often the tenderness on further examination will be found to be situated in and not beneath the abdominal wall. In a paper on "Intercostal Neuralgia as a Cause of Abdominal Pain and Tenderness,"¹ I described a test which we will apply to this patient to differentiate between parietal and intra-abdominal tenderness. We ask the patient

to make a straining effort in order to tense her abdominal muscles as rigidly as possible. If her lesion is situated inside the abdomen I will not be able to demonstrate any tenderness because her

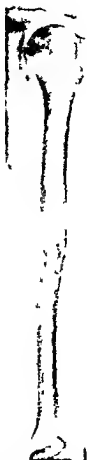


Fig. 4—Lesions in right humerus, glenoid, acromion and clavicle on February 19, 1926. Compare with Fig. 5.



Fig. 5—Pathologic fracture of right humerus, September 4, 1926. Fracture not present in radiogram taken on August 12, 1926.

rigid muscles prevent my touching her viscera. I now reapply firm pressure with my finger ends over the previously tender area. I do not indent her rigid muscles and yet the patient ex-

hibits the same distress as when her muscles were relaxed and my fingers dipped deeply into her left abdominal cavity. This proves that her tenderness is parietal. Tenderness is present over the rigid muscles of the entire left half of the abdomen and to a very considerably less degree on the right side. You will



Fig 6—Metastases in left humerus and glenoid in October, 1925. Compare with Fig 7 to note progression of disease.



Fig 7—United pathologic fracture of left humerus, July 19, 1926.

also note that tenderness is present in a band one inch in width in the upper left thigh, paralleling Poupert's ligament, the thigh area supplied by the inguinal branches of the ilio-inguinal nerve. She is not tender on much heavier pressure elsewhere over the thigh and legs. She has a V-shaped area of tenderness over the upper left buttock in the area supplied by the iliac branches of

the twelfth intercostal iliohypogastric, and ilio-inguinal nerves. She also has marked tenderness to finger tip pressure over every intercostal space from the first to the eleventh, most marked on her left side. Firmer pressure by flat fingers over the chest wall does not produce pain. Her skin, fat and muscles of both arms



Fig 8—Deposits in right radius



Fig 9—Deposits of left lower humerus and upper radius

are free from tenderness on pinching except at and near the left posterior axillary fold in the area supplied by the left intercostohumeral nerve, which you will recall is formed mainly by the first and second intercostal nerves. All these manifestations of tenderness are due to involvement of intercostal nerves. We

often see exactly the same picture in patients who do not have cancer. Commonly there is an associated superficial tenderness demonstrable by picking up a liberal fold of abdominal skin and fat and pinching it between a thumb and two fingers. Our patient does not exhibit this tenderness. Wide-spread tenderness of the abdominal parietes may be due to a variety of lesions which cause irritation or inflammation of the intercostal and first lumbar nerves. In several cases of parietal abdominal tenderness, in patients without malignant disease, microscopic examination of resected intercostal nerves failed to show any organic changes. In one case of breast cancer with metastases to the thoracic vertebræ the intercostal nerves under the microscope exhibited degenerative changes very similar to those seen in advanced alcoholic neuritis. I suspect our patient's intercostal and first lumbar nerves have undergone similar changes due to pressure of crumpled vertebræ or to actual invasion of the nerves by cancer at or near the spine. Notwithstanding extensive triangular compression of the bodies of numerous vertebræ, she does not present any other neurologic symptoms. This patient's pains have not been benefited by radiation applied over the vertebræ. Occasionally intercostal nerve pains can be abolished by radiation in the vertebral region in cases of spinal metastases. We had one striking case of breast cancer with vertebral metastasis whose intercostal nerve pains were so severe that she was bedfast on admission, but after radiation she was freed from pain for two years, during which time she did the entire household work for a family, but then died of visceral metastases.

The two ulnæ, the two fibulæ, and the bones of the wrists, hands, ankles, and feet were the only bones of our present patient that did not exhibit x-ray evidence of metastasis in late September, 1926. Notwithstanding the extensive metastases to the bone-marrow, this patient's blood-count on admission was hemoglobin, 68; red blood-cells, 4,150,000; and white blood-cells, 10,200; and a few days ago it was hemoglobin, 64; red blood-cells, 2,900,000; and white blood-cells, 9500. Her Wassermann test is negative, and her blood chemistry is normal except that in the past few weeks her blood-urea nitrogen has risen from 11 and 12

up to 24. This patient is now so emaciated and weak that she is apt to succumb from her disease or from some intercurrent infection in the near future. Were she to live another several months the disease would almost certainly continue its peripheral spread and finally involve every bone in her body.

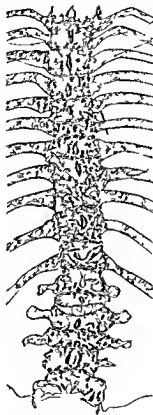


Fig. 10.—Diagram from x rays of second thoracic to sixth lumbar vertebrae.

Writers on bone metastases in breast cancer agree that involvement of subjacent ribs occurs by direct extension but they are divided in their opinions as to whether distant bone metastases occur through the blood stream or by way of the lymphatic system. Even before Handley propounded his theory of lymphatic permeation in breast cancer many writers had pointed

out various objections to the theory of cancer cell emboli in the blood-stream being the usual cause of wide-spread bone-metastases. The objections have been summarized by Handley in his book on "Cancer of the Breast," and I will not repeat them.

My clinical and postmortem observations, unsupported however by adequate microscopic studies, afford convincing proof of the correctness of the majority of Handley's views on the spread

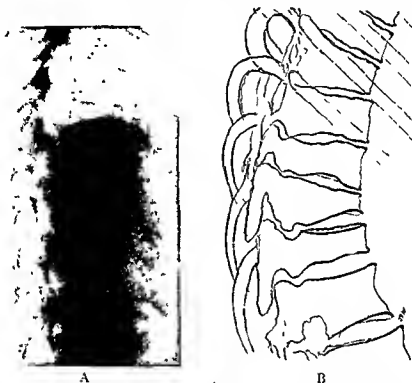


Fig 11 —Lateral x-ray (A) and sketch (B) of tenth thoracic to fourth lumbar vertebræ. Triangular compression of eleventh, twelfth, second, third, and fourth vertebræ

of breast cancer. In some directions, however, my observations have led to conclusions somewhat at variance with Handley's theories. For instance Handley expressed the belief, both in his book and in a recent personal interview, that the dissemination of cancer within the pleural and abdominal cavities is due mainly to transpleural and transcelomic transplantations, whereas, I believe lymphatic permeation is almost or quite as important within those cavities as it is in the superficial tissues.

I also believe that lymphatic permeation of cancer cells from the breast to the humerus and femur commonly follow somewhat different routes than those described by Handley. This distinguished investigator's studies were made before the days of the x ray and his original conclusions on bone metastases were based on studies of pathologic fractures and limited autopsy investigations which necessarily represented the latest stages. Our x ray studies on living patients reveal the conditions at a much earlier stage and give us a different conception of the origin of bone metastases.

Many of Handley's conclusions on bone metastases are based on a study of 329 autopsies on cases of mammary cancer at the Middlesex Hospital during the thirty years from 1872 to 1901. Among these 329 autopsies there were 6 cases in which one or both humeri were the seat of deposits. In 5 of these attention was directed to the bone by the presence of the fracture. In 4 other cases there was fracture without any definite proof of the presence of growth. The site of predilection of these humeral fractures was the midpoint of the bone at the deltoid insertion. The upper half of the humerus is so well clothed by muscles that the deep fascia lies nearest the bone at the deltoid insertion. Handley expressed the belief that the earliest metastasis to the humerus is caused by cancer cells which permeate the deep fascial lymphatics and penetrate the bone at the level of the deltoid insertion and then spread up and down the shaft from that level.

Many of our skiagrams of early invasion of the humerus demonstrate involvement of the humeral head and absence of cancer in the shaft at or near the insertion of the deltoid. The majority of the skiagrams taken during or shortly after this early stage of humeral head metastases also show early invasion of the glenoid and acromial processes of the scapula. Usually, but at a somewhat later stage the skiagrams will reveal metastases in the outer end of the clavicle. Our x ray evidence indicates that metastases to the scapula and clavicle are far more common from breast cancer than is indicated by the literature on this subject. These x ray films illustrate the preceding statements,

they together with numerous similar films disprove the theory that primary invasion always takes place at the deltoid insertion. Our roentgenologist is instructed to include the shoulder girdle on the same side as the breast lesion in the skiagram of the chest that is always taken to discover possible metastases to the lungs or intrathoracic lymph-nodes in our cases of late breast cancer.



Fig. 12—Lower lumbar vertebrae, sacrum, innominate bones, and upper femora riddled with metastases, February, 1926

As Handley has pointed out, thick muscles tend to prevent permeation from the deep fascial lymphatic plexus to the head of the humerus, hence the latter is almost certainly invaded by some other route. I believe the invasion takes place by a lymphatic permeation beginning in or around axillary lymph nodes which first became cancerous by lymphatic embolism. The almost simultaneous appearance of metastases in the humerus and ad-

jacent scapular processes followed shortly by invasion of the outer end of the clavicle strongly support this theory. Cancerous invasion of these bones (and also of the pelvic bones and femora) is always far in advance of subcutaneous nodules and is usually independent of their appearance which facts imply that cancer cells invade these bones by some other route before the slow moving permeation from the distant breast has had time to invade the fascial lymphatics overlying them. By lymphatic embolism cancer cells reach the axillary lymph nodes in close



Fig. 13—Lower pelvis and femora. October, 1925. Note progress on of metastases by comparison with Figs. 12, 14, and 15.

proximity to the shoulder joint very early and far in advance of the more slowly progressing permeation. I agree with Handley that the cancer cells involve the humerus by the process of lymphatic permeation, but I believe the route they commonly follow is beneath the deep fascia instead of superficial to the deep fascia as described by Handley in his book.

Clinical evidence indicates that permeation and embolism extending from the axillary lymphatics along the infraclavicular and supraclavicular lymphatics beneath the deep fascia are responsible for invasion of the cervical vertebrae and the skull.

On the occasion of his recent visit to the Philadelphia General Hospital, Mr Handley was shown some of our x-ray films of early metastasis to the humerus in which only the head of the bone was involved and he generously agreed that the evidence indicated that humeral metastasis could occur by permeation beneath the deep fascia. Mr Handley was very much interested in the patient whom you have just seen as she is the



Fig 14—United pathologic fracture of right femur, September, 1926

first cancer of the breast patient he has ever seen in whom bone-metastasis was demonstrated below the knee or the elbow. She has involvement of both tibiae and both radii. We were also able to show him a second patient in the ward who had metastases in both radii and both tibiae secondary to a cancer of the breast.

In the 329 autopsies on breast cancer Handley found records of 14 cases of metastases to the femur. Four of the cases were bilateral, making a total of 18 cancerous femurs. In 9 cases one

or both femora with or without fracture had proven deposits. In the remaining 5 cases spontaneous fracture gave presumptive evidence of metastasis. From a study of these late cases Handley concluded that (1) the secondary cancerous deposit in the femur always commences in the upper third and never in the distal portion of the bone (2) there is strong evidence that the great



Fig. 15—Pathologic fracture of left femur united by profuse callus. September 1926

trochanter is the point of first invasion and (3) invasion of the femur first occurs at or near the great trochanter because this part of the bone is in closest proximity to the deep fascia along which spreads the centrifugal permeation from the breast.

Our roentgenologic examinations of the femur demonstrate as shown by these films that (1) the earliest point of invasion

may be in the head and neck of the femur and not necessarily at the great trochanter, and (2) the cases which have early femoral metastasis often exhibit invasion of one or more of the pelvic bones and also of one or more (commonly two or three) of the lumbar vertebræ—the second and third being most commonly affected. I have seen numerous cases of metastases to the femur and a few extending to the tibia and one even to the met-



Fig 16—Deposit head of left tibia



Fig 17—Lower right femur, patella and upper tibia deposits

atarsus of both feet but in only one of them was I able to detect any subcutaneous nodules as low as the level of the umbilicus. The one exception was a case seen within the past month in which there were metastases to both femora and subcutaneous nodules, shown by the microscope to be cancer, within 3 inches of each ankle. I can conceive of a combination of deep fascial permeation and lymphatic embolism causing metastasis to the femur in rare instances, but I do not believe cancer cell- us-

usually confine themselves to the deep fascial plane of the body surface in making their journey from the breast to the femur. At autopsies on cases of breast cancer either with or without metastases to the bones of the spine, pelvis, and thighs I have repeatedly observed very obvious cancerous enlargement of the lymph nodes lying along the aorta (celiac and lumbar nodes), the common and both external iliac arteries (iliac nodes) and both internal iliac arteries (hypogastric nodes) and in two recent cases the cancerous nodes even extended along both femoral arteries and appeared in the saphenous region in each thigh. This commonly observed retrograde involvement of the lymphatics along the posterior wall of the abdomen extends into the pelvis long before subcutaneous permeation nodules reach the upper abdomen and I believe it furnishes the clue to the course which the cancer cells follow in the more distant part of their journey from the breast to the lumbar vertebrae to the pelvic bones and to one or both femoral heads and necks. In other words I believe the cancer cells which invade the femur usually arrive from the interior of the pelvis rather than from the superficial aspect of the deep fascia overlying the great trochanter. Mr. Handley conceded that cancer from the breast might invade the femur by the above route after being shown (1) some of our x-ray films in which the metastasis to the femur was confined to the head and neck, and (2) one autopsy in which the lumbar iliac and hypogastric nodes were invaded by cancer.

Handley further found that pathologic fracture of the femur occurred in 6 cases on the same side as the breast lesion and in only 2 cases on the opposite side. He regards the preponderance of homolateral fracture of the femur as evidence that the cancer cells traveled from the breast to the femur by way of the deep fascial lymphatics and not by way of the blood stream. It seemed to me that his 8 cases were too few in number to eliminate the element of chance as a big factor in the relative frequency of homolateral and contralateral femur metastasis.

Following Handley's visit to Philadelphia I carefully examined with Dr. Pancoast the skiagrams on 27 cases showing metastasis to the femur secondary to breast cancer on my

Radiologic Service. Examination of the skiagrams revealed one fallacy in relying upon fracture as a major index of femoral involvement. In several cases the more advanced bone metastasis was found in the femur on the side opposite to the unilateral fracture. Our skiagrams revealed a metastasis to the femur which was bilateral in 19 cases, contralateral in 3, and homolateral in 4. All the preceding 26 cases had skiagrams taken of both femora. There was one additional instance of homolateral metastasis in which the opposite femur was not x-rayed. These 27 patients were all very late or terminal cases.

Dr. Henry K. Pancoast kindly collected the data on 12 of his breast cases in which a considerable part of the skeleton had been skiagraphed at the University of Pennsylvania Hospital. His cases were in part ambulant patients and in part hospitalized patients representing an average stage somewhat earlier than in my patients. He found the metastasis to the femur was bilateral in 8 patients, contralateral in 2, and homolateral in 2.

Dr. George E. Pfahler found on eight ambulant—hence earlier stage—breast cases extensively skiagraphed at his private office that the femoral metastasis was bilateral in 1, contralateral in 3, and homolateral in 4.

Of the total of 46 patients in whom both femora were skiagraphed the metastasis was bilateral in 28, contralateral in 8, and homolateral in 10. An additional homolateral metastasis was found in one patient in whom the opposite femur was not skiagraphed. These figures show such a preponderance of bilateral invasion that the slight disparity in favor of the homolateral as opposed to the contralateral femur sinks into insignificance. I venture to predict that in a larger series the unilateral invasion will be found about equally divided between the homolateral and contralateral femurs. These facts, however, are not an argument in favor of blood-stream embolism. On the contrary, the much more frequent bilateral involvement of the upper femur with absence of involvement of bones below the knee (except rarely after extension to lower femur) is very strong evidence against blood-stream emboli. The figures quoted are quite in accord with my theory that permeation

follows along the intra abdominal and intrapelvic lymphatics in order to reach the femur

The lumbar spine was x rayed in 38 of the above 47 cases and was found to be the site of metastasis in 24. The pelvis was x rayed in 43 of the 47 and showed involvement in 34.

In my own very late group of 27 cases x rays were taken of both the lumbar spine and the pelvis in 19 and only 1 pelvis and 4 lumbar spines were found to be negative.

Although Handley attaches the utmost importance to lymphatic permeation as the method by which cancer cells from the breast gain entrance to the abdomen he largely abandons permeation in favor of transcelomic implantation as the dominant factor in the dissemination of cancer cells after they have gained entrance to the abdominal cavity.

Intra abdominal transplants undoubtedly occur and in large number in some cases but in many others probably in the great majority I believe the metastatic lesions are due to permeation. I likewise believe that permeation is a much more important process than transplantation in the dissemination of cancer cells within the thoracic cavity. Mr Handley has not been willing to concede these points of view but I hope by further correspondence to convince him of their correctness. Autopsies on cases of late cancer of the breast furnish abundant evidence of dissemination by permeation in the thoracic and abdominal cavities. In the last 8 consecutive autopsies on breast cancer that I have attended the retroperitoneal lymph nodes along the aorta and the various iliac arteries were invaded by cancer. In 3 cases in which deposits in the pelvis (ovaries and Douglas culdesac) were probably due to transplants the involvement of lymph nodes was quite similar to the 5 cases in which there were no intraperitoneal deposits in the pelvis and lower abdomen. The celiac and lumbar nodes were the largest, implying but not proving that they were the first invaded and the nodes were progressively smaller in size down to the deep inguinal (iliac) and saphenous nodes. Invasion of these nodes very certainly did not result (1) directly from transplants, nor (2) from blood stream emboli nor (3) from lymphatic emboli in those

cases in which there was neither pelvic nor lower abdominal deposits nor any subcutaneous deposits below the level of the ribs. It seems entirely plausible that these chains of glands are progressively invaded from above downward by a lymphatic permeation which extends fairly rapidly against the lymph stream. We are hoping to determine by microscopic examinations whether these nodes are invaded by permeation of the main lymphatic channels—which seems improbable because of the antagonistic strong lymph current—or by permeation of the retroperitoneal plexus of smaller channels. In several instances of breast cancer including the patient I have just shown you I have been able to palpate hard indurated lymph nodes in the saphenous regions and in two of those that came to autopsy cancer was shown by microscopic examination. It is possible that cancerous enlargement of saphenous nodes may occur sufficiently early in some instances that their presence may be the only demonstrable contraindication to the radical removal of a relatively late breast cancer.

There are several possible pathways between the primary breast lesion and the lumbar glands but they are usually not demonstrable at autopsies. Handley mentions three routes by which cancer cells may gain entrance to the abdominal cavity. (1) In those cases in which pleural deposits are present cancer cells may be conveyed by permeation or embolism through the lymphatics which arise on the pleural surface of the diaphragm and drain downward into the lumbar nodes. (2) By lymphatic permeation cancer cells may spread from the breast along the subcutaneous tissues to the lumbar region where they may pass through the posterior abdominal wall and permeate the retroperitoneal lymphatics ultimately reaching the lumbar nodes. (3) After permeation from the breast along the deep fascias to the epigastric notch cancer cells may penetrate the anterior abdominal wall and invade the lymphatic plexus of the peritoneum. From this point Handley applies his lymphatic permeation theory only to extensions to the liver and portal glands and I believe wrongly ascribes practically all other intra abdominal metastases to transcelomic implantations. I will

repeat that I believe permeation in the spread of breast cancer is just as important a process inside the abdomen as it is along the deep fascial planes of the surface of the body

The routes which the cells take from the epigastric peritoneum to the lumbar nodes are usually not determinable by naked eye examination and I have not attempted a solution of this question by

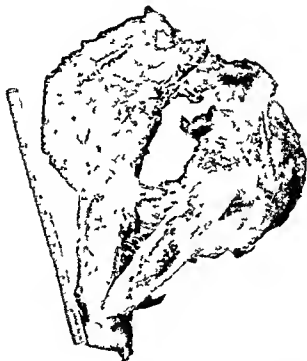


Fig 18 —Postmortem long tudinal section of un treated pathologic fracture of right femur

microscopic means In 1 case however there was a flat subserous deposit in the epigastrium with numerous small shot sized subserous deposits along the left anterior lateral and posterior parietes to the midline at the level of the lumbar nodes without corresponding deposits on the right side In another case in which the chest was free except for 1 tiny nodule in the pericardium and another

in the lung where these 2 structures rested on the left diaphragm permeation from an epigastric deposit extended mainly upward and around the under surface of the diaphragm, where small deposits were visible around to the posterior parietal peritoneum. Permeation in this case caused a subserous deposit 2 inches in diameter on the stomach and a second smaller deposit on the serous surface of the intra abdominal esophagus. In other cases permeation apparently followed along the falciform ligament to reach the portal and lumbar nodes. In 2 cases of extensive intrathoracic metastases without involvement of diaphragmatic pleura and without visceral involvement within the abdomen the lumbar nodes apparently were invaded by permeation of the lymphatics which extended along the aorta from the chest. In one of these cases the thoracic duct was extensively invaded by cancer and it may have been the route by which cancer cells reached the lumbar nodes.

The time at my disposal permits of my citing only another one or two from many additional instances in which intra abdominal or intrathoracic deposits were caused by permeation rather than by "transplantation across cavities". At a recent autopsy the lungs and pericardium were free from metastases but on opening the pericardium the epicardium was studded with numerous small deposits apparently secondary to permeation from enlarged lymph nodes lying behind the pericardium. At another recent autopsy cancerous deposits were found between fused peritoneal layers behind the upper cecum a situation absolutely inaccessible to transplants.

The patient became gradually weaker and died three weeks after being shown in the Clinic. At postmortem examination each pleural cavity contained 300 ccm of bloody fluid. The costal and diaphragmatic pleurae were studded with small discrete white hard nodules varying in size from a pinhead to a bean. Similar nodules were found on the parietal and interlobar surfaces of the lungs and a very few within the lung substance. Mediastinal lymph nodes size of a pea to cherry. Liver weighed 1480 gms. Numerous metastatic nodules up to an inch in diameter on the surface and in substance of liver, especially in right lobe.

Portal lymph nodes enlarged Spleen weighed 160 gms with nodules within its substance varying in size from a pinhead to a small marble Except for numerous rice grain sized nodules in mesentery of the jejunum and ileum there were no intraperitoneal metastases below the level of the liver

The lymph nodes along the thoracic and abdominal aorta and along the common, internal and external iliac arteries and in both saphenous regions were enlarged, and on section presented the gross appearance of cancer The largest nodes attained the size of a walnut and were situated along the sides of the abdominal aorta a short distance above its bifurcation The spinal dura was not thickened and the spinal cord was normal in size except in the lower cervical region where it seemed to be compressed by an extradural metastasis Microscopically the spinal cord did not show any organic changes No gross abnormality of the brain

Scirrhus adenocarcinoma was found by microscopic examination in the epicardium lungs spleen liver adrenal glands, ribs right radius left femur and in lymph nodes along the aorta and iliac arteries and in the saphenous regions

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CANCER OF THE PROSTATE WITH EXTENSIVE BONE-METASTASES

I WILL discuss some points in connection with cancer of the prostate ere bringing the next patient before you

Cancer of the prostate is a very common affection Young¹ estimates that 4 out of every 100 men who live to be sixty years of age will have cancer of the prostate It almost never occurs before the fortieth year Various clinicians find that cancer is present in about 1 out of every 5 patients that seek treatment for symptoms of prostatic obstruction

The usual initial symptoms are frequency and difficulty of urination and they develop more rapidly in prostatic cancer than in benign hypertrophy In the latter condition the interval between the onset of nocturia and the occurrence of marked dysuria is often three or four years, whereas in cancer it is commonly only three or four months Pain is a very infrequent symptom in benign hypertrophy in the absence of stone or infection, but is an outstanding symptom in fully one fifth of the cases of prostatic cancer when they first come under observation The pain may be located in the bladder rectum or perineum, and is then probably due to nerve pressure by the local growth Pains further afield as in the lower abdomen lower back gluteal regions and legs result from nerve pressure by metastatic deposits in the lumbar vertebræ or sacrum or in pelvic or abdominal lymph nodes

Bilateral leg pain in men over fifty years of age is commonly due to prostatic cancer In several of my cases the undue prolongation of pain in region of hip or thigh following slight trauma has led to an examination of the prostate with the discovery of an otherwise unsuspected cancer

Bone metastases are present in about one fourth of the cases of prostatic cancer by the time the diagnosis of the local lesion is made The bones first affected are those of the pelvis and lumbar

spine The most common source of metastatic carcinoma of bone in men is the prostate and in women is the mammary gland The first suspicion that a given patient has cancer of the prostate is often afforded by a skiagram—taken to ascertain the cause of obscure pains—showing characteristic metastatic bone changes Prostatic cancer is an exception to the rule that metastatic cancer usually causes destructive changes in bone The bone metastases from cancer of the prostate as a rule are markedly osteoplastic By the x ray the affected bones appear larger and denser and exhibit a characteristic chalky or ‘marble’ appearance An otherwise doubtful diagnosis of cancer of the prostate may be cleared up by a skiagram showing that the bones adjacent to it are the seat of osteoplastic metastases The surgeon should have skiagrams taken of the pelvis and lumbar vertebrae before committing himself to a definite prognosis or line of treatment in every case of cancer of the prostate

Metastases to the pelvic and lower abdominal lymph nodes are more frequent but less readily diagnosed than metastases to the bone Metastases to lungs liver spinal cord and skin are infrequent

Hematuria and pyuria are found in only 1 or 2 per cent of cases of prostatic cancer

Cancer of the prostate usually forms an indurated nodular mass easy of diagnosis by rectal palpation In its later stages indurated horns extending outward and upward indicate extension along the seminal vesicles Atypical cases occur in which the prostate is not enlarged and the only palpable evidence of cancer may be one or two small resistant but not indurated areas quite similar in feel to areas of chronic gonorrheal folliculitis In other exceptional cases the consistency of the cancer may not differ from that of simple hypertrophy and then the diagnosis is usually established only by microscopic examination after a prostatectomy

The patient who is walking into your presence is a white male aged seventy two years His present chief complaint is throbbing pain in both legs It began about five months ago and was shortly followed by persistent soreness and tenderness

rather than actual pain" in the arms, head, neck, chest, and abdomen. Pain in legs interferes with sleep and is much worse when climbing stairs.

He has had occasional attacks of dyspnea for past two years. He has had chronic cough for past three months and once coughed up bright red blood. Appetite is good and bowels are regular.



Fig. 19—Skigram of lungs which unexpectedly revealed metastatic lesions in every bone shown in the picture.

Six weeks ago he was admitted to the medical wards of this hospital. Physical examination at that time revealed carious teeth, thickened pleura, patches of chronic bronchopneumonia, slight myocarditis, marked arteriosclerosis, and other minor lesions with which we are not particularly concerned today.

Urine normal. Blood urea nitrogen normal. Wassermann test negative. Moderate anemia.

An x-ray picture of lungs (Fig. 19) taken five weeks ago un-

expectedly revealed osteoplastic changes of a chalky appearance in all of the bones included in the skiagram. The bone lesions presented the characteristic appearance of metastases from cancer of the prostate. I was requested to examine the prostate that day.

On rectal palpation I found a prostate of the size ordinarily encountered in a young adult. It was normal in consistency throughout except for one small fairly firm nodule about 1 cm. in diameter in the left lobe. The local evidence of pathology was so slight that no one would have felt more than the faintest suspicion that cancer was present had it not been for the metastatic bone evidence. The local findings have not changed appreciably since my first examination. Five years ago I would not have believed it possible that such an insignificant latent local lesion could represent a cancer of sufficiently long duration to cause the extensive bone lesions present in this patient. In recent years I have seen 4 undoubted cases with similar insignificant local findings. Two of them were treated on our Radiologic Service. Both had been examined including cystoscopy by competent urologists within one week and four weeks respectively and were pronounced free from cancer of the prostate. Both gave histories of rapid development of great frequency, urgency and distress of urination without infection and associated with pains in the thighs. One had undoubted metastasis to lungs without bone involvement and the other had metastasis to the ilium. Both were subjected to suprapubic cystostomy for relief of symptoms primarily, but at the same time glass seeds of radium emanation were implanted in the prostate and applied on its vesical surface. Biopsy from each revealed cancer. Further applications of radium by urethra and by rectum in the lung metastasis patient resulted in the disappearance of all palpable evidence of local cancer, the cystostomy was allowed to heal and the patient had normal urination for some months before he died of cachexia.

It is because of experience in such proven cases and because of the bone pictures in this patient that I am convinced that the meager local findings indicate cancer.

He was transferred to my service in the Radiologic Depart

ment about four weeks ago, since which time his entire skeleton has been x rayed

A study of these films (Figs 16 to 28) demonstrate carcinomatous metastases to the skull clavicles, scapulæ humeri, radii ulnæ all ribs sternum every vertebra entire bony pelvis and both femora It will be noted that the disease, as evidenced by the skiagrams shades off into apparently normal bone at the distal ends of the radii, ulnæ and femora A study of the skiagrams of all our cases of bone metastases secondary to cancer



Fig 20—Wide spread metastases to skull

of the prostate, justifies the general statement that metastases involve first the bones near the prostate and thereafter extend to the next adjacent bones in a gradual peripheral extension The patients commonly die before sufficient time has elapsed for demonstrable metastases to reach the bones of the hands and feet Involvement of the bones of forearms and legs (below knees) is a very late manifestation In the extremities the dis

ease first involves the proximal ends of the humerus and femur then gradually extends to their distal ends before crossing the joint line to invade the proximal ends of the next lower bones. I have not seen any instance of isolated distant bone metastasis such as Kinney² describes as occurring in the scapula. Blumer³ 1 case each in frontal bone, tibia and scapula and Bumpus⁴ 2 cases in ribs secondary to prostatic cancer. A distant isolated bone lesion is best explained by a vascular embolism of cancer cells. In a more recent paper on a clinical study of 1000 cases of



Fig. 21—Metastases to every bone shown in skiagram

carcinoma of the prostate Bumpus⁴ does not mention finding any instance of distant isolated bone metastasis. Of 539 patients examined roentgenographically the pelvis was found involved in 123, the spine in 107, making an aggregate of positive findings in approximately 25 per cent of the series. The femur was affected 16 times and the ribs 10, but always in conjunction with pelvic involvement.

The systematic peripheral spread in the osseous system ab

solutely negatives the theory of vascular embolism in the cases we have observed. Emboli originating in the systemic circulation—as well illustrated by sarcoma metastases—commonly involve the lungs primarily and profoundly; and further extensions



Fig. 22.—Deposits in right humerus, shoulder girdle, and ribs. Left humerus is shown in Fig. 21

do not follow any systematic scheme of dissemination but are characterized by haphazard deposits in widely separated areas.

Systematic dissemination beginning in the bones near the prostate and extending peripherally from bone to bone with late or

no involvement of the lungs can occur only by lymphatic permeation. The opponents of the theory of lymphatic permeation point out that the presence of lymphatics in bones has not been proven and that cancer cells have been found in the smaller blood vessels in the bones. However the presence of lymphatics within the bones is not essential as cancer cells may permeate to the surface of the bone by the periosteal lymphatics. Multiplying cancer cells in other structures and regions tend to follow pre existing channels (as in the milk ducts of the breast) and on theoretical and clinical grounds it can be assumed that they would follow the same procedure by extending through osseous channels from the surface into the haversian canals and into the marrow cavity. The site of the invasion of blood vessels could be within the bone itself. In other words vascular invasion might very well be the result rather than the cause of bone invasion. These theories however need microscopic confirmation.

It is by no means proven that lymphatics are absent from bones. Of recent writers I will quote Piney⁶ who was able to inject the lymphatic channels in the periosteum with comparatively little difficulty the injection material passes from these channels into the bone and from it into the endosteum but I have been quite unable to find any evidence of a connection between these periosteal endosteal lymphatics and the marrow tissue. I disagree with Piney's view that cancer cells are carried to the bones as emboli in the blood stream. Piney lays stress on the blood picture resembling that of profound pernicious anemia in cases of extensive bone metastases. The blood count on this patient taken two days ago was hemoglobin 67 red blood cells 3 440 000 and white blood cells 7300. Differential count showed Polys 71 Lymphos 19 Large Monos and Trans 4 Eosins 5 Basophiles 1. Another differential count a week earlier was essentially the same except no eosinophiles were found. As a rule we have not found the very grave anemias described by Piney in our cases of extensive bone metastases. By the injection of dyes into the marrow cavity of the femur and humerus in dogs Kolodny⁷ was able to demonstrate a dye stained lymphatic trunk passing through the cortex near the upper end of

each of these two bones. He also demonstrated the dye in the regional lymphatic nodes which in the case of the femur corresponded to the external iliac and hypogastric lymph-nodes in man, and in the case of the humerus corresponded to the supra-



Fig 23 —Deposits in left radius and ulna Fig 24 —Fourth thoracic to third lumbar vertebrae

clavicular lymph-nodes in man. It is quite possible that the lymphatic trunks described by Kolodny may be the channels by which cancer cells invade the head and neck of the femur and humerus, which as we shall discuss presently is the usual site of first in-

vasion of bone in the extremities Kolodny states that deviations from the normal in the flow of lymph namely the aberration of the lymph stream and the reflux lymph flow can lead to the metastatic spreading through the skeleton of carcinomatous cells transported in the lymph circulation from the primary tumor Kolodny's studies are important evidence in favor of lymphatics being present in the bone marrow but I believe he



Fig. 25 — Pelvis and lower lumbar vertebrae

is at fault in completely ignoring the process of lymphatic permeation as a factor in bone metastases

Metastases beginning in bones near the primary focus and gradually extending peripherally from one bone to the next adjacent bone is apparently a more uniform process in cancer of the prostate than in cancer of the breast. This seeming variation is due to the anatomic differences in the lymphatics surrounding the prostate and the breast. From the prostate lymphatic extensions (embolism and permeation) lead first to the pelvic

bones and lumbar spine, whereas in the breast, under varying conditions, the lymphatic extensions may first encounter bone (1) in the axilla on the same side causing involvement of the shoulder girdle bones (p 18), (2) within the abdomen along the aorta causing invasion of the upper lumbar vertebræ (p 23), or (3) within



Fig 26 —Upper right femur

the chest lymphatic permeation along the third, fourth, or fifth interspace (from internal mammary nodes or from a pleural invasion by direct extension through the chest wall) producing disease of the third, fourth, and fifth thoracic vertebræ (p 48)

The site of primary bone invasion thus differs in prostatic and mammary cancer, but in both of them invasion of the bones

of the extremities commonly occurs first at the upper ends of the humeri and femora and gradually extends down them before invading the upper ends of the bones below the elbow and knee. The route taken by the cancer cells in passing from one bone

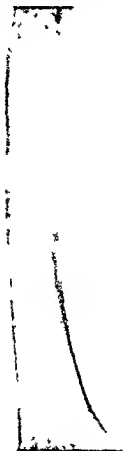


Fig 27 —Left femur



Fig 28 —Right femur

across the elbow or knee joint line into a more distal bone is not known but the almost invariable absence of associated cutaneous and subcutaneous nodules near the elbow and knee indicate that it is by lymphatics which lie deeper than those on the superficial aspect of the deep fascia.

Although microscopic demonstration is wanting, the clinical evidence points to the deep lymphatics being the routes by which cancer cells spread from the prostate to the bones of the chest and skull. No one has explained, satisfactorily, the amazing predilection for metastases to the bones in cancer of the prostate.

After being shown in the Clinic, the patient remained free from urinary symptoms and was out of bed walking each day for

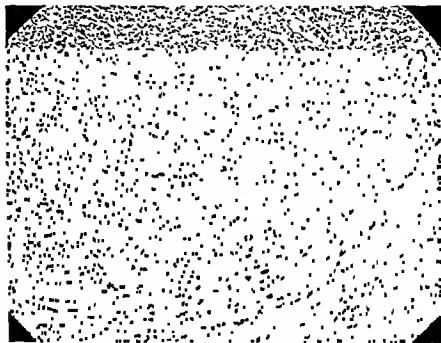


Fig 29 —Prostate Low power

two weeks when he developed a convulsion and died a few hours later.

The autopsy findings checked by microscopic examinations revealed adenocarcinoma of the prostate (Figs. 29, 30) and metastases to lymph-nodes surrounding the lower portion of the abdominal aorta, to skull, ribs, sternum, and femur (Fig. 31); to lungs and pleuræ, both very recent, and to the posterior lobe of pituitary body and the left gasserian ganglion.

A strip of deep fascia extending from the crest of the ilium to a point below the knee was removed, but without observing the precautions outlined by Handley,⁸ and was examined mi-

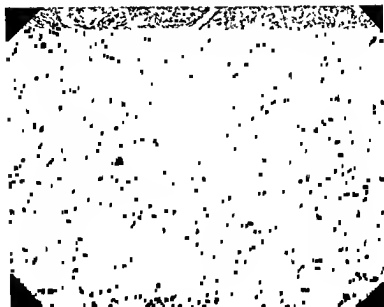


Fig 30—Prostate High power



Fig 31—Metastases in femur

croscopically at numerous levels for cancer cells, but none were found. Large cancers of the prostate often obstruct the ureters and cause death from chronic uremia. In this patient the blood-urea nitrogen was normal shortly before death and the kidneys and ureters were practically normal at autopsy, hence his terminal convulsion was not due to kidney insufficiency. The convulsion and death were probably caused by the metastatic tumor at the base of the brain, and the tumor itself apparently originated by direct extension from the osseous deposits in the base of the skull.

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CLINIC OF DRS JOHN BERTON CARNETT AND N W WINKELMAN

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METASTATIC TUMORS OF THE NERVOUS SYSTEM

THIS colored female was admitted to the Radiologic Department of this hospital on July 27, 1926. After much deliberation she gave her age as thirty six years, but that is an understatement by ten or fifteen years. She was married at sixteen and has two children.

At some uncertain period in the summer of 1924 she discovered a small hard lump in the right breast. A few months later a cancer quack applied caustic paste over the breast for a period of three weeks. The resulting ulcer never healed. She has not had any other treatment. Within the month obstinate constipation and abdominal distension have led to the use of powerful cathartics. Following a bath three days before admission her feet felt "chilly and numb". The following morning she was unable to stand because of weakness in both lower extremities and she experienced a sensation of "numbness" and "needle point stickings" in both legs and knees.

On admission, region of right breast was represented by an ulcerating area which was 4 inches in diameter and fixed to the chest wall. Large lymph nodes in right axilla. Heart and lungs normal. Abdomen distended and tympanitic. She had complete paralysis of both lower limbs except for slight movement of the left toes. Abdominal, knee and plantar reflexes were absent. Sensation of all forms was lost from the level of the zyphoid downward. Control of rectum and bladder was lost. These symptoms indicated a lesion about the level of the fifth or sixth thoracic vertebra.

An x ray film of the spine (Fig. 32) disclosed cancerous metastases and crushing of the bodies of the fifth sixth and seventh vertebræ. The upper thoracic vertebræ (usually one or two higher than in this patient) are a common site for the first



Fig. 32 — Metastases to fourth fifth sixth and tenth thoracic vertebræ

appearance of bone metastases in cases of late breast cancer. Handley ascribes their involvement to lymphatic permeation beginning in the lymph nodes along the internal mammary artery and extending outward and backward between the ribs. In passing I might mention that some years ago Handley extended his

breast operation to include excision of the internal mammary lymph-nodes, but the increased mortality caused him to abandon excision and adopt radiation of these nodes by use of radium needles at the time of operation to safeguard against late recurrences from this source.

In this patient the breast is firmly fixed to the chest indicating a direct extension of the disease to and into the chest wall possibly reaching the subjacent parietal pleura, so that permeation of her intercostal lymphatics may have started from there rather than from the internal mammary nodes

The x-ray film also revealed metastasis in the tenth thoracic vertebra which probably became invaded by cancer cells from lymph-nodes along the thoracic aorta

The rapid or sudden development of a paralysis at a given cord level, with x-ray evidence of triangular compression of the bodies of carcinomatous vertebræ at the same level, is often interpreted as signifying that the paralysis occurred coincident with the crushing of the vertebræ and is being continued by direct compression of the cord by the deformed vertebral body or bodies. Paralysis may occur by this mechanism but it must be rare

Postmortem investigation of our cases of paralysis—even when they exhibit the usual sudden onset of symptoms—indicates that the lesion is commonly due to a metastatic extradural tumor which may act by direct compression of the cord but much more frequently acts by shutting off the blood-supply to the cord.

On the assumption that the paralysis in this patient might be due to cord pressure by a metastatic extradural tumor she was given four applications of radium emanation each amounting to 5000 mc. hours at 10 cm. distance with $\frac{1}{2}$ mm Ag. and 2 mm. brass filtration over the fifth to the eighth thoracic vertebræ at three-day intervals beginning August 9th.

About two weeks after the fourth treatment she began to show an improvement which has continued so that she is now able to walk into your presence. For the sake of future paralytics we hope that the improvement in her case is due to the radium rather than to "nature."

I have asked Dr Winkelman our neuropathologist to come here today for a two fold purpose First I want him to demonstrate the present neurologic symptoms in this patient and second I want him to tell you at first hand the results of his post mortem studies of a few of our cases of metastatic tumors of the cord and brain I take great pleasure in introducing Dr N W Winkelman

I made a complete neurologic examination of this patient yesterday and will not bore you by repeating all of the tests at this time The patient is now free from pain She has complete control of her bladder and bowels As you see she is able to walk unaided although very slowly Her tendency to stagger a little in all probability is due mainly to weakness rather than inco ordination Her knee and ankle reflexes are about equal, and are neither exaggerated nor depressed There is no movement of the toes at all on stroking the sole of either foot Sensations of all sorts are perceived normally

In a review of 20 cases of metastatic tumors of the nervous system 2 very similar spinal cord cases proved to be of such great interest and importance in explaining a symptom complex that it might not be out of the way to enter into a discussion of them at the present time Everyone has seen cases where during the course of carcinoma somewhere in the body especially in the breast and prostate a paralysis of the lower limbs has resulted At times this paralysis has come on suddenly It is about such cases that our discussion is concerned

It is well known that the spinal cord can escape injury even when a marked deformity of the spine exists such as occurs in Potts disease and in secondary or even primary tumors of the vertebra Then there is a second group of cases with weakness or paralysis below a given level without demonstrable involvement of the spinal column And finally a third group occurs in which while the Roentgen ray does show nothing of one or more of the bodies of the vertebrae deformity has not occurred and still clinical evidence of a partial or complete transverse lesion occurs To explain the last two groups of conditions we have been able to study the following cases

Our first patient was a colored man of forty eight who was admitted to the genito urinary section of the Philadelphia General Hospital, October 15, 1924, because of difficulty of urination which came on shortly after an operation for supposed appendicitis. Two weeks before admission he went to bed feeling as well as usual but upon attempting to arise in the morning he found his lower limbs were paralyzed and his legs felt "dead." He had no pain and no girdle sensation. Upon examination a moderately enlarged soft prostate was found. There was a flaccid paralysis in both lower limbs. Plantar stimulation produced flexion on both sides. From the upper third of the thighs downward sensation of all forms was decreased. Retention of urine was complete.

He was transferred to the neurologic service of Dr. Lloyd, who found flaccid paraplegia retention of urine, requiring daily catheterization and atrophy of the muscles of the paralyzed limbs. He complained of paresthesias from the lower costal margins to the iliac crests. Sensation in all forms was impaired below the tenth thoracic segment to just below the knees. From the knees downward sensation was entirely lost. Above the tenth thoracic segment there were no neurologic symptoms. He developed decubitus grew progressively worse became septic and died. At necropsy a primary carcinoma of the prostate was found with metastatic lesions in the lungs liver, perihilar and retroperitoneal lymph nodes and a flat extradural tumor on the posterolateral surface extending from the seventh thoracic level to the conus. At no point was the tumor thicker than 2 or 3 millimeters. Microscopic examination showed the tumor to be an adenocarcinoma. There was an incomplete transverse softening of the spinal cord in the lower thoracic region (7-9 segments) with ascending and descending degenerations of the cord. The softening was due to occlusion of the blood vessels by the tumor. The vertebræ were not involved.

In this case the size of the tumor would immediately suggest that the cord lesion could not possibly have been due to the tumor itself without implication of the blood vessels. In this case as in the two previously reported by Spiller the damage to the cord

was sudden in onset and due to shutting off of the blood supply to one or more segments of the spinal cord

In our second case the paralysis was likewise sudden in onset and occurred while in the hospital under our observation. She was a white woman of forty two admitted to the Philadelphia General Hospital service of Dr. Carnett March 26 1926 and died May 17 1926. In an attempt to rid her face of superfluous hair six years ago roentgenologic treatments were given twice weekly for seven months. One year after the last treatment an x ray wart appeared on the chin. With treatment it apparently disappeared but recurred. Three attempts were made to excise it the last time by cautery but it came back two months before admission. For a time radium treatment controlled it but soon the glands in the neck became involved. It was at this time that she came to the hospital for lead treatments.

On physical examination a diffuse scar was found on the chin and neck in the midst of which was a necrotic looking mass. The cervical lymph nodes were enlarged hard and fused. Three days after admission she received her first ampule of lead intravenously with apparently slight improvement in the local condition of the neck. Ten days after the second injection she began to complain of pains in the left chest at the level of the eighth and ninth ribs. Five days later she suddenly developed a complete motor and sensory paralysis below the umbilicus. The sensory level gradually ascended until it reached the level of the fourth intercostal space prior to her death one month after the sudden occurrence of the paraplegia.

Roentgenogram studies had shown a suspicious area in the eleventh thoracic vertebra. At postmortem the brain was grossly normal. On the removal of the spinal laminae a gelatinous mass was found surrounding the cord extradurally from the sixth to the twelfth thoracic segments. Compression of the cord had not occurred but the cord substance was soft and mushy and the anatomic markings were lost. Microscopic examination showed the tumor to be carcinomatous probably of the melanotic type. The spinal cord itself was softened beyond recognition.

In this case also direct pressure on the spinal cord had not

occurred but the clinical phenomenon of a sudden onset of a motor and sensory paralysis can be very easily explained by compression of the blood vessels supplying the cord

It is to be emphasized in conclusion that in both of these cases while extradural tumors of the spinal cord were found, the involvement of the spinal cord itself was due to stoppage of the blood supply rather than direct pressure on the cord substance. And in both cases the clinical course fits in with the pathologic interpretation

The following cases are illustrative of involvement of the brain and its membranes

Case I—A white woman aged thirty seven was admitted to the Philadelphia General Hospital February 24 1924 on the service of Dr. Carnett and died August 5 1924. In April 1923, a tumor was removed from the right breast. In October she complained of pain in the head. During the winter of 1923 1924 she noted a lump in the other breast which later became painful. In February 1924 she suddenly became delirious and complained of severe occipital headache and dimness of vision. Neurologic examination revealed double ptosis the pupils were dilated irregular slightly unequal and fixed. There was marked choking of both disks. The retina of the right eye revealed hemorrhages. The spinal fluid was clear and contained no abnormal constituents. The Wassermann reaction in both blood and spinal fluid was negative. Some time after admission she developed a right astereognosis and a right hemiparesis. There was a double Babinski sign with subjective complaint of numbness in the right upper limb. After a few weeks she became blind. Roentgenologic examination of the head at this time gave negative findings. She showed progressive mental deterioration failed physically and died.

At necropsy there was noted a scirrhous carcinoma of the left breast (the right breast had been amputated). Metastatic lesions were present in the brain (Fig. 33). They were located in the left paracentral lobule and right thalamus extending

downward into the subthalamic region and the midbrain, in the posterior part of the right occipital lobe and in the corpus callosum

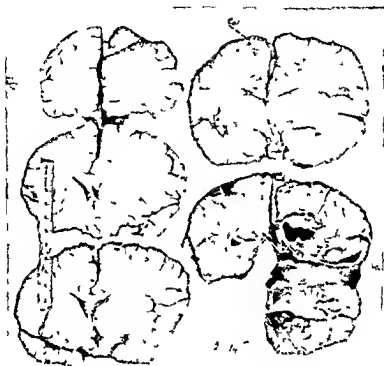


Fig 33 —Co Carcinomatous tumor masses.

Case II —A white woman, aged fifty four, was admitted to the Philadelphia General Hospital May 4, 1923, on the service of Dr C H Potts and died in eight days. She was picked up on the street, wandering about in a dazed condition. On admission to the Hospital she could give no connected account of herself. It was learned that she worked in a shirt factory on the day of admission, but had not been well for about three months. She had complained of double vision, thick speech and weakness of the right face. Both breasts had been removed, one in February, 1918, and the other some time later. There was no evi-

dence of local recurrence, but there were some enlarged glands along the carotid vessels. In walking she staggered to the left. The left pupil was larger than the right, both reacted sluggishly. The deep reflexes were present and normal. Plantar stimulation produced flexion on the left and extension on the right. The legs

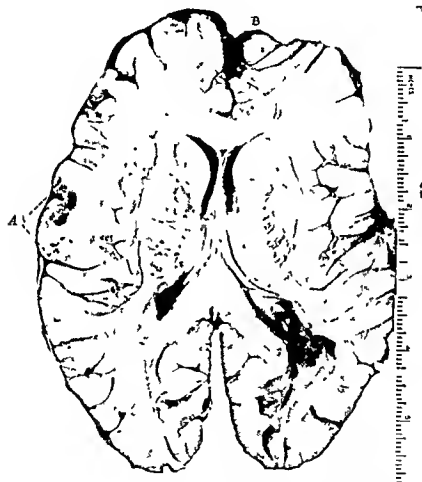


Fig. 34—Shows petechiae at A. A similar area at B was removed for microscopic examination.

were very sensitive to pressure. While in the hospital she had a series of convulsions associated with twitching of the right side of the face. The sphincters were intact. Lumbar puncture revealed a clear fluid, under normal pressure. The Wassermann tests, in both blood and spinal fluid, were negative. The urine

showed a trace of albumin. The blood chemistry was normal. Eight days after admission she became stuporous and died. The twitching of the right side of the face continued to the time of death.

At the postmortem examination petechial hemorrhages of the brain, especially of the left motor areas for the face and arms and the right frontal area were found (Fig 34). Microscopically the blood vessels throughout the brain, especially the smaller

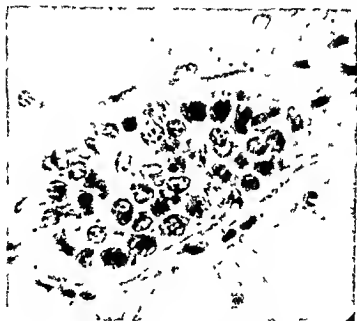


Fig 35 —Cancer cells within a blood vessel

ones, contained cancer cells (Fig 35). In the left lower motor zone the cancer cells had perforated the vessel wall and extended into the nerve tissue. Metastatic nodules were present in the lungs and in one rib.

Case III —A colored woman, aged sixty one, was admitted to the Philadelphia General Hospital February 13, 1925, on the service of Dr. Carnett and died one month later. She had had

12 children and 4 miscarriages. In March, 1923 she noticed a lump in the left breast with enlargement of the axillary glands four months later. In November she developed paralysis of the right side of the face. A short time later the right sixth nerve became involved. Following this she developed cough and dyspnea. Later there was difficulty in swallowing and occasionally

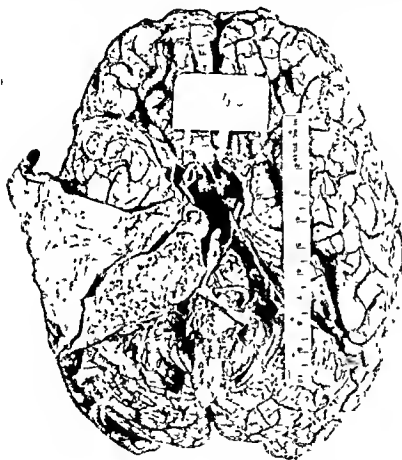


Fig. 36—Carcinomatous nodule at base of brain

food would regurgitate through the nose. In one year she lost 30 pounds. In February, 1925 both optic disks showed swelling. Neurologic examination at that time showed involvement of the fourth to the twelfth cranial nerves inclusive on the right side, and weakness of the right arm. The tendon reflexes were all present and normal. In March, 1925 she had a convulsive

seizure which began in the right arm. She became stuporous and died from hypostatic pneumonia. The blood Wassermann test was negative. There was a trace of albumin in the urine. The blood chemistry was normal.

At necropsy a tumor of the breast with metastatic nodules to the axillary, mediastinal and abdominal lymph nodes and to the lungs and the liver was found. Microscopically the breast tumor was a squamous cell carcinoma. The brain (Fig. 36) showed a nodular growth invading the dura of the under surface of the right temporal lobe, extending backward to the anterior edge of the cerebellum and occupying the right cerebellopontile angle, compressing all the cranial nerves in this region.

Case IV—A white woman, aged forty seven, was admitted to the University of Pennsylvania Hospital on the neurosurgical service of Dr. Frazier January 5, 1926. Her breast had been removed for carcinoma four years before. She made a good recovery and at the time of admission there were no signs of local recurrence. Late in 1925 she began to complain of headache. Later there developed general weakness and attacks of vomiting. Neurologic examination on admission showed both disks to be slightly swollen. She had marked occipital headache and frequent vomiting spells. There was slight cerebellar incoordination on the left side. A diagnosis of left cerebellar tumor was made. Operation by Dr. Frazier revealed a firm, well defined tumor in the left posterior fossa which was removed intact. It measured 3 by 3.5 cm. It had compressed the left cerebellar lobe. Microscopic examination showed it to be a scirrhous carcinoma. The patient made an excellent recovery, but months after discharge from the hospital was showing evidences of metastatic lesions in other parts of the body.

We have here illustrated four different types of lesions, all resulting from primary tumors in the breast. In the first case the metastatic lesions were within the substance of the brain itself, producing pressure and necrosis of the nerve tissue as the tumor expanded. In the second case while no actual macroscopic tumor could be seen the blood stream was filled with cells that were

cancerous In the third case the metastatic nodule was attached to the under surface of the dura and produced its damage by compression of the emerging nerve roots In the last case the tumor was isolated and easily removable at operation, and differed in no way macroscopically from an endothelioma Microscopic examination alone made the differentiation

CLINIC OF DRS E B KRUMBHAAR AND J P SCOTT

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TUMORS OF THE SPLEEN WITH A REPORT ON TWENTY-EIGHT RECENT CASES

Occurrence —Tumors of the spleen are of especial interest on account of their comparative rarity and the relation that this may have to the supposed role of the spleen in opposing neoplasms. As this question has been discussed at some length in a recent article by one of us¹ it will suffice here to say that experimental evidence also supports the view that splenic and neoplastic tissues are antipathetic in that tumor grafts 'take' less often and are smaller than in other organs and tissues, and that intrasplenic tumor inoculation is most efficient in raising general resistance to later inoculation (Lazarus Barlow and Parry²). At certain periods after splenectomy, too, the organism seems to be more susceptible to tumor growth. Both clinical and experimental evidence make it clear that the resistance is relative, not absolute and probably varies greatly in different individuals and conditions.

In several cases of carcinomatosis we have found nodules grossly diagnosed as metastases which microscopically showed fibrous tissue with few or no neoplastic cells, this raises the question as to whether or not the spleen may at times be able to deal with tumor metastases by a fibrosing process. Sappington³ reports a case of carcinoma of the breast, in which the splenic sinuses were crowded with tumor cells and agrees with Deelman and Kettle⁴, that careful microscopic examination would more often reveal splenic metastases. It should be pointed out, however, that cells within the blood stream do not constitute metastatic growth and that tumor cells can be injected into or found in the

circulation without necessarily causing tumor growth. Mechanistic reasons that have been advanced to explain the rarity of splenic tumors are that lymphatics exist only near the capsule so that implantation must be mostly by the blood stream that the sharp angle of the splenic artery tends to keep out tumor cells and that the pulsations of the spleen hinder their lodgment.

Of the benign tumors fibroma lymphoma lymph and hemangioma have been observed and of the malignant tumors primary endotheliomas large round cell and lymphosarcoma and primary and secondary carcinoma. Primary carcinoma is found in the older literature only and it is difficult to see from what splenic tissue it could arise other than some ectopic epithelial rest. Gaucher's disease is no longer considered neoplastic.

In the complete autopsy records of this hospital splenic neoplasms are mentioned eighty five times. As so many of these are early reports however and unsatisfactory for various reasons the findings in the last five thousand (5000) autopsies are more valuable. In this series twenty eight splenic neoplasms occurred of which all but two were accompanied by satisfactory data. Of these fourteen were secondary carcinomata three lymphosarcomata secondary to lymphoid tumors four melanosarcomata secondary to skin lesions two endotheliomata that had arisen in lymph nodes two primary sarcomata a hemangioma and a lymphangioma and a sarcomacarcinoma arising in the small intestine.

Etiology—In a review of 104 cases of primary malignancy of the spleen Smith and Rusk⁵ found a history of malaria in 13 per cent of the cases lues in 4 per cent trauma in 4 per cent tuberculosis in 2 per cent and typhoid occasionally. These percentages are small however and it is reasonable to assume that the usual causes of malignancy whatever they may be are operative also. In the secondary tumors propinquity is one factor and another seems to be the frequency of lung metastases—hence the frequency of metastasis in breast cases with propagation via the arterial system. Of 29 cases of secondary carcinoma in which the evidence was reasonably satisfactory of the whole

series of 16 000 autopsies, ten arose in the stomach five in the pancreas, four in the right breast three in the left, two in the liver, two in the gall bladder, and one each in the penis ovary, and rectum Of the fourteen secondary carcinomata of our shorter series, the primary lesions were in the breast in 5 cases, in the stomach and pancreas respectively in 3 cases and in lip, prostate and penis in 1 each In only 2 cases was tumor appearance in the spleen by direct extension in the rest apparently by invasion from the blood stream

BENIGN TUMORS

Fibromata are extremely rare and little more than pathologic curiosities Occurring as small single or multiple nodules they cause no symptoms and require no treatment

Angiomata may be either lymph or hemal in kind The two in our series (one of each kind) were inconspicuous autopsy findings but from the occasional reports in the literature (Steden, Naher⁶) they may reach enormous size giving a soft palpable, perhaps irregular tumor with some discomfort and ascites Only in such cases need surgical intervention be considered

Lymphoma and lymphadenoma are described as 'small, single or multiple, circumscribed collections of lymphoid cells, sometimes surrounded by a connective tissue capsule They probably represent instances of localized hyperplasia of the malpighian bodies" (Lyon) and should not be confused with sarcoma or leukemia

MALIGNANT TUMORS

Secondary carcinoma is undoubtedly the commonest form of malignant involvement of the spleen but, occurring late in a widespread process its recognition is of but little clinical value If it has occurred by extension from a neighboring organ, the spleen is usually adherent to the infiltrated connective tissue and lymph nodes and the process is diffuse and extensive being most marked nearest the capsule Metastasis by the blood stream may produce a single small circumscribed firm, whitish nodule or numerous large nodules that occupy more than half the sub

stance of the organ or any intervening stage. The tendency of small nodules to fibrose and of microscopic lesions to occur which are invisible grossly has already been mentioned. The enlarged spleen may be palpable and cause symptoms but it is of course then too late to attempt more than palliative treatment.

Sarcoma—Whether in the form of small or large round cell fibro angio or lymphosarcoma endothelioma or splenocytoma (Lino⁷) sarcoma though very rare constitutes the most important primary tumor of the spleen. Opinion is divided as to the relative frequency of these varieties and as to how individual cases should be diagnosed. Thus Smith and Rusk agree with Mallory⁸ that lymphosarcoma is the commonest type and regroup many of the cases reported in the literature, while Ewing⁹ favors endothelioma and MacCallum¹⁰ warns that tumors of doubtful origin are especially liable to be branded endothelioma. These primary tumors are more apt to be single and may cause the spleen to become very large (over 5 kilos) with very little splenic tissue remaining. They tend to be more or less circumscribed vary considerably in appearance and texture and may contain broken down cysts. Primary endotheliomata have been reported occurring multiple nodules. Angiosarcoma should be easy to distinguish histologically while Risel¹¹ claims that careful study will permit endothelioma to be traced to the endothelium of the sinuses.

Secondary Sarcoma especially lymphosarcoma (which may be part of a general body process rather than a truly secondary tumor) is commoner than the primary form but less easily diagnosed. It can be dismissed with the same remarks as were made about secondary carcinoma. It seems as if melanosarcoma perhaps on account of its extremely high virulence was particularly prone to metastasize in the spleen. In 4 of our 5 cases and both of Dawson's¹² cases of melanosis the spleen was involved.

Symptoms—The spleen is often considerably enlarged in the primary tumors and frequently nodules can be palpated and the customary notch lost. Pain in the left side persistent or intermittent, may be accompanied by pain in the back and left shoulder

or over the abdomen generally. It may appear late or be entirely absent. The enlarged spleen is usually but not necessarily tender. Signs of gastric indigestion, flatulency, and constipation are usually present with emaciation and the other signs of malignancy developing rather rapidly. Secondary anemia is usually marked. Pleural effusion was present in 16 per cent, ascites in 20 per cent of Smith and Rusk's series. Jaundice and anasarca have occasionally been noted, also fever and leukocytosis. In secondary metastasis the splenic involvement is usually marked by the primary process.

Diagnosis—Rapidly of growth, especially with an irregular splenic outline, may suggest a proper diagnosis, but if the various signs just described are waited for it will be too late for any treatment to be of use. Splenic puncture has been known at least once to have caused rupture and should not be tried. Practically all the causes of enlarged spleen must be considered in differential diagnosis.

Treatment—Prompt removal of the spleen offers the only chance of saving life in the primary cases and as an enlarged spleen is better out of the body in many other conditions as well, an exploratory operation is the more advisable in doubtful cases. Of 39 splenectomies in Smith and Rusk's series 7 died as a result of the operation. Of the other 32 11 were known to have developed metastases in periods varying from five weeks to nine years after the operation. The remaining 21 were free from recurrence when last seen, though as is always the case with such figures many were reported all too soon after operation. Unquestionably this operative mortality could be reduced, but even as it stands operation affords a decidedly preferable alternative to the quick and certain death of expectant treatment.

CASES

PRIMARY CARCINOMA

Case 1—L. L. (Aut. 8868 Dr. Saleeby), white, male, fifty-five, admitted with digestive disturbances and constipation of about a month's duration. He was slightly dyspneic and jaundiced and very tender on both sides of the epigastrium. The

spleen was just palpable. Cholecystectomy was followed by pleural effusion and a mistaken diagnosis of subphreinc abscess. Death occurred three months after admission.

At autopsy, the spleen was greatly enlarged and weighed 625 gm. At the upper pole was a firm, depressed, yellowish mass, and tough grayish strands branching from the hilum into the splenic tissue joining other discrete or confluent nodules, some of which had a semi-solid center. Altogether more than half of the organ was occupied by tumor tissue. Microscopically the tumor cells were large, oval, irregular, deep staining cells and

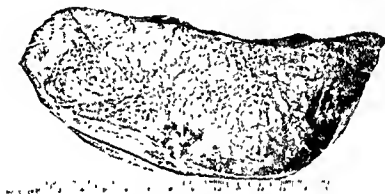


Fig. 37—Case 1 Primary sarcoma of spleen (Aut. 8868)

very anaplastic, supported on a scanty fibrous stroma, but surrounded by dense fibrous tissue. An identical growth was present in the lymph-nodes, but a more diffuse process in the lungs and pleura. The liver, diaphragm, pancreas, and stomach were also involved.

Diagnosis.—Large round cell sarcoma, primary in spleen.

Case 2.—M. B. (Aut. 7247, Dr. Konzelman), negress, seventy-five, an old hemiplegic, was found at autopsy to have in the upper pole of the spleen, a pale red, homogeneous, sharply defined firm nodule, 2 cm in diameter. Microscopically this presented a homogeneous appearance moderately well defined from the adjacent splenic tissue. Numerous oval and spindle

cells were found with considerable pink staining intercellular substance and many small thin walled blood vessels

Diagnosis—Primary sarcoma (early, not producing symptoms)

SECONDARY LYMPHOSARCOMA

Case 3—J R (Aut 5467, Dr McCutcheon) a white man aged sixty one, admitted May 15, 1920 presented signs and symptoms referable to lymph node enlargements in the neck, groin, mediastinum and abdomen for over a year. Under x ray treatment the masses in the neck and chest practically disappeared in twenty four hours but later returned and resisted further treatment. He had a terminal fever (100° to 102° F) slight leukocytosis (10 to 12 000 with lymphocytes 28 per cent), and anemia (red blood cells 2,400 000) and was emaciated.

At autopsy, the spleen which weighed 360 gm contained very minute white nodules and microscopically showed like the lymph nodes, a destruction of the normal structure by a "proliferation of large round cells of the endothelial type many of which are quite large and pale."

Diagnosis—Lymphosarcoma, secondary to multiple (?) lymph node tumors



Fig 38—Case 4 Secondary lymphosarcoma of spleen (Aut 6988)

Case 4—M L (Aut 6988, Dr Lucke), white male fifty nine, was admitted August 25 1922 complaining of a palpable movable mass in the right abdomen loss of weight for three months (40 pounds) and nausea and vomiting soon after meals

Cystoscopy showing blockage of the right ureter the diagnosis of sarcoma of kidney was made. There was considerable anemia (red blood cells 2 600 000) and marked urine changes (cloud of albumin blood cells epithelial and granular casts)

At autopsy the abdominal mass consisted of matted mesentery omentum and loops of intestine the lymphoid tissue of which seemed to be the primary site of the neoplasm with metastases to the kidneys liver pancreas and spleen. The spleen which weighed 160 gm was slightly enlarged and contained four circumscribed white tumor masses varying from 8 to 20 mm in diameter which microscopically consisted of large oval cells with vesicular nuclei and scanty cytoplasm.

Diagnosis Secondary lymphosarcoma arising in lymphoid tissue of intestines

Case 5—F W B (Aut 10 031 Dr Borman) white male thirty three was admitted greatly emaciated and in such severe pain that a history and physical examination were unobtainable. He had a large slightly movable tumor in the left hypochondrium extending to the level of the umbilicus.



Fig 39—Secondary lymphosarcoma of spleen (Aut 23 52)

At autopsy the mass was found to arise from retroperitoneal lymph nodes with the spleen extensively adherent on its under surface and metastases to the lungs and peribronchial lymph nodes liver diaphragm and spleen. There was a bilateral

pleural effusion and ascites The spleen which weighed 90 gm, showed several small whitish nodules on the adherent under surface (by extension) which microscopically, like the parent tumor, showed infiltrating tumor cells that were large, oval or polyhedral with large anaplastic deeply staining nuclei, varying in size, many mitoses and scanty cytoplasm

Diagnosis—Secondary lymphosarcoma arising in the retro peritoneal lymph nodes

SECONDARY ENDOTHELIOMA

Case 6—R B (Aut 8059 Dr Gilmour) white male, twenty three, was admitted August 20, 1923, complaining of swollen glands in the neck for eighteen months, weakness, anemia and pain in his feet At biopsy a supraclavicular node was diagnosed as Hodgkin's disease The patient was in a very poor condition (red blood cells 1,540 000, leukocytes 4500) and died a month later

At autopsy the lungs, liver and spleen showed similar lesions which were with difficulty diagnosed from Hodgkin's disease The irregularity in size, shape and depth of staining of the predominant cell absence of eosinophiles and typical Reed giant cells sparsity of plasma cells and discrete metastases in lungs, liver and spleen finally determined the diagnosis of endothelioma The spleen which weighed 590 gm contained several firm flesh colored growths, microscopically of the same nature as the neoplastic process in other tissues and in addition quite distinct typical miliary tubercles with Langerhans giant cells and with and without caseation

Diagnosis—Secondary endothelioma arising in cervical lymph nodes

Case 7—J S (Aut 8072, Dr Lucke) black male twenty five was admitted September 14 1923 with an atypical bronchopneumonia, from which he died two weeks later Both liver and spleen were palpable

At autopsy the spleen, which weighed 325 gm, showed innumerable dark red spots 1 to 5 mm in diameter, many with

a central yellow spot and surrounded by a narrow yellow rim. An enlarged lymph node nearby showed a similar appearance, but not the liver. Microscopically, however, while the lymph-node was almost completely occupied by a tumor cell similar to that of Case 4, only occasional small nests of such cells were found in the spleen, the gross lesions being minute hemorrhages in process of organization.

Diagnosis—Secondary endothelioma (microscopic) arising in abdominal lymph-node.

SECONDARY SARCOMA

Case 8.—F. F. (Aut. 6666, Dr. McCutcheon), white male, forty-eight, was admitted with pain in the back and abdomen and abdominal distention of two months' duration. After paracentesis a large mass was palpated above the umbilicus, which at autopsy two weeks later was found to arise in the small intestine.



Fig. 40—Case 8. Sarcocarcinoma of spleen, arising in intestine. Gross lesion (Aut. 6666).

Autopsy showed a complex tumor, arising from the ulcerated small intestine, matting together the abdominal viscera and spreading by extension to the liver and spleen. Sections from various parts of the neoplasm showed two kinds of predominating cells, one with deep staining vesicular nucleus arranged in acini and strongly suggesting an epithelial origin, the other fibroblastic



Fig 41—Sarcocarcinoma of spleen, arising in intestine Histology of sarcomatous portion, upper half, normal spleen below ($\times 276$)



Fig 42—Sarcocarcinoma of spleen, arising in intestine Histology of carcinomatous portion ($\times 276$)

in appearance or more frequently as a spindle shaped fibrillar cell of mature type arranged in irregular whorls which contain many small blood vessels with poorly formed walls. The spleen which weighed 135 gm had its surface partly covered by the new growth which extended 7 mm into the surface.

Diagnosis—Sarcocarcinoma arising in small intestine

SECONDARY MELANOMA

Case 9—F B (Aut 7191 Dr Schochet) white female seventy four observed on her right elbow a pigmented mole which soon began to enlarge four years before admission. The next year a lump appeared on the right side of the neck and then in many other places over the body. She gradually became weak developed mental symptoms and died one week after admission.

At autopsy metastatic growths were found throughout the skin and in the lungs pancreas intestines brain lymph nodes and spleen. The spleen which weighed 160 gm contained in the lower pole a circular nodule 2.5 cm in diameter with a dark gray necrotic center and a yellow gray periphery. Microscopically the small spindle shaped cells arranged as in sarcoma were accompanied by very little melanin pigment.

Diagnosis—Secondary melanoma arising in a mole on the elbow

Case 10—L M S (Aut 9700 Dr Eaman) white female fifty six was admitted moribund with a melanoma of the right labium and extensive metastases.

At autopsy metastases were found in the skin heart lungs liver kidneys adrenals brain and spleen. The spleen was about twice its normal size and studded with small nodules throughout. These showed typical polyhedral cells with a moderate amount of pigment.

Diagnosis—Secondary melanoma arising in vulva

Case 11—H P (Aut 8901 Dr Hartman) white male forty five was admitted in poor condition with numerous tumor

nodules in the skin, arising from a pigmented mole in the back, which he had scratched a year before.

At autopsy, numerous nodules were found in the skin, lung, kidney, adrenal, liver and spleen. The spleen, which weighed 255 gm, contained three small nodules 0.5 to 2.5 cm in diameter. Microscopically the usual spindle or polygonal, pigment-bearing cells with abundant mitoses were found.

Diagnosis—Secondary melanoma, arising in skin of back.



Fig 43—Case 13. Primary hemangioma of spleen, photomicrograph (Aut 7234)

Case 12.—C. J. (Aut. 9976, Dr Borman), negro, sixty, had had for an indefinite period a large pigmented area on the sole of the foot, 5 cm. in diameter, surrounded by a callous and numerous more recent nodules over the body. Death occurred a few days after admission.

At autopsy metastases were found in the skin lungs liver kidneys adrenals testicles bladder lymph nodes bones and spleen. The spleen which was slightly enlarged showed no distinct nodules but the cut surface (like that of the liver) was bluish black with dirty black fluid scrapings. Microscopically in both organs innumerable deeply pigmented cells were found in the sinusoids—either diffuse tumor cell infiltration, phagocytosis of melanin by reticulo endothelial cells or both.

Diagnosis—Melanosis arising from a pigmented node of the sole of the foot

ANGIOMA

Case 13—M B (Aut 7234, Dr Schochet), white female thirty one a case of dementia præcox died of generalized tuberculosis

At autopsy, on one surface of the spleen, which also contained tubercles was a small cavernous angioma, with spaces lined by flattened endothelial cells containing debris but no blood cells. It was therefore thought to be of lymphatic origin (See photo micrograph)

Diagnosis—Lymphangioma

Case 14—C D (Aut 7460 Dr Freeman) white male thirty one died of cardiorenal disease and terminal broncho pneumonia

At autopsy the atrophic spleen was found to contain a cavernous angioma full of blood. No further details are included

Diagnosis—Hemangioma

In both these cases the diagnosis is of pathologic interest only

SECONDARY CARCINOMA

PANCREAS

Case 15—R E (Aut 5313 Dr McCutcheon), white male seventy-four, was admitted in an advanced stage of carcinomatosis and died soon after

At autopsy the primary lesion was found in the middle of the pancreas with metastases to liver and spleen. The spleen which

weighed 120 gm., showed no nodules grossly, but occasional nests of tumor cells like those of the parent tumors were found microscopically.

Diagnosis.—Early secondary carcinoma, arising in the pancreas.

Case 16.—R. J. (Aut. 5555, Dr. McCutcheon), white male, forty, was admitted with a diagnosis of brain tumor and died in five days.

At autopsy the primary lesion was found in the pancreas, with metastases to the abdominal wall, kidneys, adrenals and spleen. The spleen, which weighed 130 gm., showed two hard yellowish nodules, 1 cm. in diameter, resembling the secondary nodules seen in other organs. Unfortunately, the sections taken for microscopic examination apparently did not include a nodule.

Diagnosis.—Secondary carcinoma, arising in the pancreas.

Case 17.—A. E. (Aut. 8122, Dr. Morgan), negress, fifty-seven, was admitted with digestive disturbances and palpable masses in neck and abdomen.

At autopsy a large adherent mass was found in left abdomen, embracing the pancreas, spleen, left kidney, great vessels and stomach. The primary lesion was found to be in the tail of the pancreas. The spleen was densely adherent to the upper pole of the left kidney. It contained a hard whitish mass, 2 cm. in diameter in the center and near the hilum, which microscopically consisted of dense fibrous tissue, containing strands of tumor cells and scattered cells in the loose spaces that occurred near the margin of the mass. The picture is suggested of repair of a metastatic growth.

Diagnosis.—Secondary carcinoma, arising in the tail of the pancreas.

STOMACH

Case 18.—(Aut. 6026, Dr. Lucke), white male, fifty-two, had had difficulty in swallowing food with regurgitant vomiting for three months and a larger swelling in the epigastrium with sharp pain and rigid abdomen for one month. He was constipated

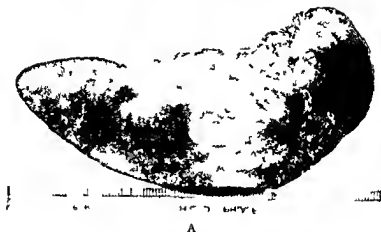


Fig 44—Case 18 Secondary carcinoma of spleen arising in stomach
A Gross B photomicrograph X 276 (Aut 6026)

and had lost 40 pounds. Operation revealed a diffuse carcinomatosis. Jejunostomy was performed and the patient died two days later.

At autopsy, an adenocarcinoma of the cardiac end of the stomach was found with metastases to the gastric and mesenteric lymph-nodes and the spleen. The spleen, which weighed 270 gm., showed a number of pale gray-brown nodules, varying from a few mm. to 2.5 cm. in diameter, and constituting about one-half the organ. It was not adherent. Microscopically the nodules were composed of epithelial tumor cells tending to form imperfect acini.

Diagnosis.—Secondary adenocarcinoma, arising in cardia

Case 19.—A. F. (Aut. 7570, Dr. Freeman), white male, thirty-five, was admitted with advanced inoperable carcinoma of the stomach.

At autopsy, an interstitial carcinoma of the "leather bottle" type was found with metastases to the esophagus, lungs, pleuræ, intestines, mesentery lymph-nodes, bladder and spleen. The splenic involvement, however, consisted merely of one or two small nodules attached to the capsule, made up of the predominant tumor cells and representing part of the general peritoneal carcinomatosis.

Diagnosis.—Secondary carcinoma of splenic capsule, arising in the stomach.

Case 20.—N. C. (Aut. 7361, Dr. Lucke), white male, thirty-nine, died from a hemorrhage from an ulcerated carcinoma of the pylorus of unknown duration.

At autopsy, metastases were found chiefly in the liver, peritoneum and perirectal lymph-nodes, also in the diaphragm, lungs and spleen. In the spleen, involvement, however, consisted merely of a few small tumor nodules attached to the capsule—part of the general peritoneal carcinomatosis.

Diagnosis.—Secondary carcinoma of splenic capsule arising in the pylorus.

BREAST

Case 21—C G (Aut 6010 Dr Case) white female, seventy seven, had a scirrhus cancer of the breast for five years, recurring after operation and on admission had palpable nodes in the axilla and was much emaciated

At autopsy, two weeks later, metastases were found in the lungs liver and spleen The spleen, which weighed 160 gm, contained a number of circumscribed, pale red nodules 2 to 3 mm in diameter many with a whitish center Microscopically these were composed of cords of oval and round tumor cells, varying considerably in size, shape and depth of staining

Diagnosis—Secondary adenocarcinoma, arising in the breast

Case 22—A L (Aut 6952 Dr Lucke), white female, seventy one had had her left breast amputated for cancer two years before admission without recurrence On admission she was much emaciated and had copious signs of metastases in the lungs and died three weeks later

At autopsy the primary lesion in the breast was found to be healed, but metastases were found in the lungs, liver, left adrenal and spleen The spleen, which weighed 145 gm, contained a slightly projecting white nodule, 2 cm in diameter near the upper pole which microscopically showed a medullar growth of large oval epithelial cells with abundant cytoplasm The nuclei were pale and many showed nucleoli with a few mitotic figures

Diagnosis—Secondary carcinomatous nodule, from a medullary cancer of the breast

Case 23—M W (Aut 7597, Dr Hartmann), negress thirty-six, admitted moribund and greatly emaciated, with an ulcerated cancer of the right breast of a year's duration

At autopsy the next day, metastases were found in the lungs, liver and spleen While the lungs and liver were studded with nodules, the spleen, which weighed 145 gm, contained a single whitish nodule, 1 cm in diameter, which on section proved to be a true metastasis

Diagnosis—Carcinomatous nodule in spleen, secondary to breast

Case 24—M H (Aut 7941 Dr Strumia) white female, forty five, was admitted moribund with extensive cancer of both breasts

At autopsy, the adenocarcinoma of the right breast was found to have metastasized to the left breast lungs uterus and spleen. The spleen, which weighed 520 gm was practically filled with dark round nodules, infiltrating the pulp and scattered over the capsule, with a microscopic picture resembling the parent tumor

Diagnosis—Secondary adenocarcinoma, arising in right breast

Case 25—F F (Aut 8240, Dr Morgan), white female fifty-five, was admitted much emaciated with general carcinomatosis of obscure onset more than a year before

At autopsy, the primary growth was apparently a hard walnut sized tumor in the right breast, with extensive metastases throughout the skin of the body lungs, pleuræ myocardium, pericardium, diaphragm, peritoneum pancreas adrenals thyroid, bladder and spleen. The spleen, which weighed 145 gm, and was free of adhesions, was studded with hard purplish gray nodules through the substance of the organ, which when near the surface pushed the capsule up into projecting nodules. Microscopically, the tumor cells were round or cuboid with marked evidence of gland formation

Diagnosis—Secondary adenocarcinoma, arising in the right breast

This case is interesting on account of not only the extent of the metastases, but the presumable hematogenous origin of the splenic nodules, while lymphogenous spread was plain in other metastases

LIP

Case 26—E B, (Aut 7693, Dr McGinnis), white male, sixty, had had lesions on his lower lip and right angle of the mouth, which for six months had been treated by his physician

with washes and ointments. On admission the large ulcerated cancers were accompanied by large metastases in the right submaxillary and submental lymph nodes. Following radiation (total 3858 m c hours) and a fairly heavy reaction with inflammation the lower lip lesion improved but the others progressed. Six weeks later further treatment to the right half of face and neck (884 m c hours) was followed by cellulitis and eventual removal of a mass of necrotic material. Thereafter the patient's general condition improved and he felt but little pain though the lesion steadily progressed.

At autopsy metastases were found in the lungs bronchial and mediastinal lymph nodes liver kidneys and spleen. The spleen which weighed 210 gm contained a few hard nodules about 1 cm in diameter which microscopically reproduced the picture of the primary growth.

Diagnosis—Secondary nodules arising from a prickle cell carcinoma of the lip.

PENIS

Case 27—T C (Aut 8447 Dr Eiman) white male seventy six first noticed difficulty on urination in February 1922 when sores appeared on both sides of the glans. The penis was amputated and inguinal nodes excised in March and all went well until August 1923 when the stump suddenly broke down. In spite of fulguration on admission to this hospital there was a large ulcerated carcinomatous area about the stump and obvious nodules in both groins and thighs so that radium treatment was not considered suitable.

At autopsy besides the lesions described there were metastases in lungs pleuræ heart liver kidneys lymph nodes and spleen. The spleen which weighed 120 gm showed one small nodule which was apparently not included in the section taken.

Diagnosis—Secondary nodule arising from prickle cell carcinoma of penis.

PROSTATE

Case 28—R A (Aut 8506 Dr Eiman) negro sixty six had had burning frequent bloody micturition for six months and some loss of weight. The firm fixed enlarged prostate led to a

diagnosis of carcinoma of that organ, which was confirmed at operation and 24 bare tubes of radium (1584 m c hours) inserted. Death occurred four days later.

At autopsy, metastases were found in the bladder, seminal vesicles, ureters, and spleen. The spleen, which weighed 110 gm., showed numerous bluish-gray nodules studded through its pulp, the largest 1.5 cm in diameter, which microscopically showed the same anaplastic cells with tendency to acinous formation.

Diagnosis.—Secondary nodules, arising in adenocarcinoma of the prostate.

We are indebted to the various interns, chiefs, and pathologists of this hospital for the material used in this study.

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CLINIC OF DRS HENRY K PANCOAST AND
JOHN L GOFORTH

RADIOLOGIC DEPARTMENT, PHILADELPHIA GENERAL HOSPITAL

RECURRENT ENDOTHELIOMA OF TENDON SHEATHS OF
FOREARM WITH PULMONARY AND PROBABLY CEREBRAL METASTASIS

THIS case is of particular interest because of the unusual nature of the neoplasm and the variety of opinions expressed as to the identity of the tumor by a large number of eminent pathologists

Male, aged twenty-seven years, colored Our first experience with this patient was August 25, 1924, when he was referred to the x-ray Department of the University Hospital from the Surgical Out-Patient Department for an x ray examination of his right forearm following an injury two days before, caused by striking his elbow against a wall while lifting a stone He thought the stone fell against his arm with considerable force At the time of our examination there was a healed scar over the ulnar aspect of the forearm about 10 inches long At the upper end of the scar there was a small swelling

The roentgenogram of the forearm showed an unusual oblique fracture of the shaft of the radius at the upper and middle thirds There was nothing in the appearance at the time to suggest that it was pathologic

The lump at the upper end of the scar grew rapidly subsequent to the injury, and at the time of his admission to the surgical ward of the University Hospital, September 22d, it had grown to the size of a man's fist It was nodular, rather soft, and slightly tender to pressure. The epitrochlear and axillary lymph-nodes were moderately enlarged, soft, and movable A

second Roentgen-ray examination of the forearm on the day of admission showed little or no callus or union of the fracture (Fig 45). Because of slight rarefaction at the ends of the fragments, best shown stereoscopically, and the presence of the rapidly growing soft tissue tumor we now thought the fracture might have been a pathologic one. A Roentgen-ray examination



Fig 45

of the chest on the same day showed a well-defined metastasis to the lungs, with one large nodule in the left base and numerous very small suspicious nodules throughout both lungs (Fig 46). This was regarded as a probable metastatic sarcoma from the forearm tumor, although the exact connection between the bone lesion and the soft tissue tumor was uncertain. The clinical

diagnosis was recorded as sarcoma of the radius. A Wassermann test was negative.

On the following day a piece of the tumor on the forearm was removed for biopsy and the pathologic diagnosis based on a frozen section was round cell sarcoma. On September 25th Dr. Muller removed the entire growth by cautery excision removing with it a considerable portion of the flexor group of muscles. A large metastatic invasion was pulled out of the basilic vein, which was ligated. Dr. Bothe returned the fol-



Fig 46

lowing pathologic report after examination of sections of the growth. Section is made up almost entirely of large cells fairly uniform in size and shape. There are fine fibrous bands running throughout the entire section which divide the cells into an alveolar arrangement. There are some areas where there is marked vacuolization of these large cells.

Diagnosis —Metastatic hypernephroma

On questioning the patient, it was learned that in July, 1911, he felt something "pop" in his right wrist, and a small lump

developed and grew slowly, and was finally removed at Danville, Virginia, in February, 1923. This was soon followed by a recurrence, and, complaining of "painful swelling of the right forearm" he went to the Jefferson Hospital, Philadelphia, where a

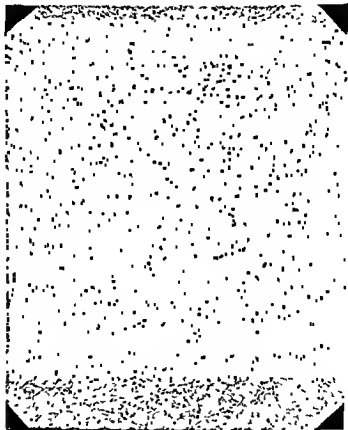


Fig. 47.—Low power view of slide preparation from the Jefferson Hospital specimen showing alveolar arrangement of growth. Fibrous strands traverse the neoplasm, forming many smaller lobules ($\times 115$)

tumor mass, measuring $9 \times 4.5 \times 2.5$ cm. was excised by Dr. J. H. Gibbon, April 3, 1923. This growth involved the flexor muscles of the forearm and was yellowish and lobulated. On section, fibrous strands separated it into small islands, and numerous red, hemorrhagic streaks were present throughout

Histologically it was composed of large, vacuolated cells with large, oval, vesicular nuclei, and prominent, deeply staining nucleoli, arranged in small alveolar groups (Fig. 47). In places tubule-like structures with lumina were seen, often forming a patterning suggestive of kidney tubules. A few blood-vessels

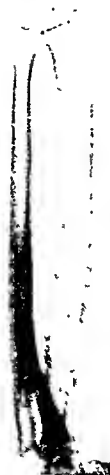


Fig 48

were noted between the alveoli. Mitoses were rare. Drs. B. L. Crawford and B. C. Crowell of the Jefferson Hospital, and Dr. F. B. Mallory of Boston, and Dr. Joseph McFarland of Philadelphia, on examining the sections prepared from this neoplasm, were of the opinion that they were dealing with a metastasizing tumor of adrenal origin, a diagnosis which was rendered by Dr. Bothe¹ on examination of the sections made from the second recurrence.

The patient was discharged from the University Hospital October 8 1924 after complete healing of the incision and was transferred to the Radiologic Service of the Philadelphia General Hospital for deep x ray therapy of the forearm chest and abdomen but was to report back to the University Hospital when this was completed

He was re admitted to the University Hospital December 13 1924 and was found to have a small doubtful recurrence A Roentgen ray examination of the forearm now showed considerable rarefaction at the seat of fracture and doubtful union Radiating spicules were noted which still further indicated that the fracture had been pathologic (Fig 48) The examination of the chest showed a little more progress in the lung metastasis A careful search was instituted for a primary focus on the basis of the pathologic diagnosis of hypernephroma but without success There were no palpable abdominal masses and pyelograms made December 16th and 23d showed normal kidney pelvis and calyces The patient was discharged December 23 1924 to return to the Out Patient Department for further observation

The peculiar behavior and unusually slow growth of the neoplasm clinically were not in keeping with the usual course of hypernephromata and although the majority of pathologic opinions favored a tumor of adrenal origin the microscopic picture admittedly was not characteristic of the neoplasm described by Grawitz^{2 3} Further pathologic studies were now made in the hope that the tumor might be definitely identified Dr Allen J Smith of Philadelphia examined sections from both the Jefferson and University Hospital specimens and concluded that the growth was endotheliomatous in nature Dr James Ewing of New York suggested tendon sheath origin for the tumor because of its alveolar and endotheliomatous appearance histologically (Fig 49) He did not regard the adrenal as being primary Dr J G Bloodgood of Baltimore gave the diagnosis of recurrent endothelioma of tendon sheath origin and also ruled out the adrenal as being primary Our study and examination of all available tissues and sections from this unusual neoplasm also led to the conclusion that the growth was

of endotheliomatous nature, a conclusion which was strengthened by the fact that we were able to demonstrate practically the same microscopic picture in several recently studied endotheliomata of pleural origin

The patient was re-admitted to the University Hospital September 22, 1925, with a well-marked recurrence of the growth

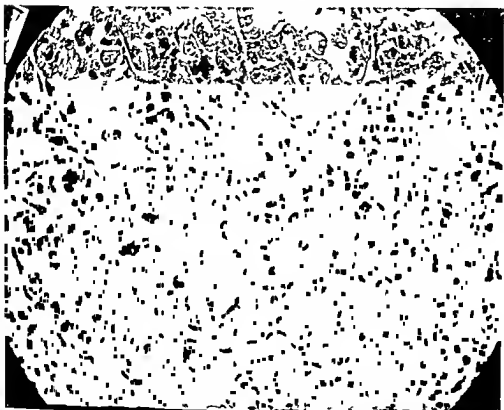


Fig 49—High power view of section from the University Hospital specimen showing several alveoli or tubule like structures. The tumor cells are large, with abundant, granular, vacuolated cytoplasm, and large, oval nuclei which contain prominent nucleoli ($\times 276$)

in the forearm. This had been increasing rapidly in size for three months and had given rise to a constant dull pain. He complained also of a slight pain in the lower right chest and had an unproductive cough. There were no abnormal physical signs over the chest. On the day of admission Dr. Ravdin performed an amputation at the lower and middle thirds of the

arm. On the day of his discharge, October 5th, a Roentgen-ray examination of his chest showed quite advanced lung metastasis (Fig 50)

He was re-admitted on the Radiologic Service of the Philadelphia General Hospital March 9, 1926, complaining of severe dull headache which had lasted two weeks. For one week he had been vomiting frequently. Spinal fluid pressure was 34 mm. of mercury. A diagnosis of intracranial metastasis was made.



Fig 50

He was presented before the conference of the Radiologic Staff April 12th. At that time he was stuporous, the pulse had dropped suddenly from 80 to 52 and his temperature from 99° to 96° F. and respirations were 11. A decompression had been proposed, but was not advised because of the advanced lung metastasis and the doubtful resulting prolongation of life that would result from such a procedure.

At the time of this writing, June 24, 1926, the patient is still alive, his mentality has cleared somewhat, but he continues to

lose ground slowly. There still seems to be no doubt that he is suffering from an intracranial metastasis.

There is every reason to believe that the forearm tumor has been of the same histologic nature since at least the very beginning of the apparent recurrence. We do not know what the original lump was that developed in 1911. If it was not a tumor, of the same nature as was found at the last two excisions, then the malignant growth started some time between 1911 and February, 1923. The tumor is being regarded by the pathologic staff of the Radiologic Clinic of the Philadelphia General Hospital as an alveolar endothelioma probably arising from the tendon sheaths of the forearm.

We realize that the tumor is an unusual one and we give due credit to the opinions of those who disagree with our own diagnosis, which necropsy will affirm or disprove. The clinical picture is to us not that of hypernephroma. Even granting the fact that primary hypernephroma has been described as originating elsewhere than from the immediate locality of the adrenals,³ the clinical aspect of this case is more that of a slower growing neoplasm, and an alveolar endothelioma is certainly a strong possibility. The secondary bone involvement near the forearm growth is more in favor of endothelioma.

Note.—As this report is about to go to press we wish to add that the patient died December 10, 1926. Autopsy revealed metastases in the cerebellum, lateral ventricle, liver, spleen, lungs, mediastinum, and heart. The kidneys and adrenals were negative, and nothing was found to suggest a primary hypernephroma. Pathological reports have not yet been received. There was a recurrence in the stump of the amputated area.

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CLINIC OF DR EDWARD S CLAYTON, JR

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MULTIPLE PRIMARY CARCINOMATA

THE infrequent occurrence of true multiple primary carcinomata and the possibility of their throwing light on the origin of tumors are items of sufficient interest to justify reporting the two following cases. One of these had three primary carcinomata and is of extreme interest.

Case 1—**H. A.** A white woman, seventy six years old, was admitted to the hospital April 2, 1925, complaining of abdominal swelling and of tumor of the left breast.

Past History—There was no family history of cancer. She had had one child fifty nine years ago. Her past medical history is of no importance.

History, Present Illness—Two years ago for the first time the patient noticed that her abdomen was getting larger and had continued to increase in size. The enlargement was not accompanied by any pain nor any discomforts other than for its size. She has been constipated as long as she can remember, but has not been more so since the abdomen has been swollen. Fifty nine years ago after the birth of her child she noticed a small painless lump the size of a pea in her left breast. She said the lump continued to enlarge for fifty nine years until at the present time it is the size of an orange. The tumor did not cause the patient a great deal of concern until during the past six or seven months it has enlarged more rapidly than at any other time. She never had any discharge from the nipple nor any discomforts from the tumor. She began to lose weight and got thinner in spite of the abdominal enlargement during the past two years. There have

been no cardiac, respiratory or gastro intestinal complaints except constipation. She has had nocturia four to five times during the past year but no other urinary complaints. Menopause occurred at forty five years of age. There was a rather sudden cessation of menses, but she had no previous menstrual complaints and no bleeding leukorrhea, or any complaints since her menopause.

Physical Examination—The patient is a rather markedly emaciated white woman seventy five years old with a very wrinkled dry skin and a sallow pale complexion. Her face looks puffy but there is no pitting on pressure. In the outer quadrant of the left breast just above the nipple is a tumor mass 8 x 6 cm. It is hard and only slightly movable. The skin over it is mottled glossy and thinned out. The growth is firmly attached to the skin but apparently not to the underlying muscles. There is some irregularity in the outline of the mass, and it is entirely painless. The axillary glands are not palpable. The abdomen is quite large and tense. Dulness is present in the flanks and extends high up on either side. No tenderness no masses or organs are felt on account of the abdominal fluid. The abdomen was tapped and 16 liters of clear straw colored fluid was removed after which the abdominal wall was flaccid and wrinkled and large irregular tumor masses could be felt and seen. These masses had a cystic consistency and were scattered throughout the abdomen. One the size of an infant's head was present in the left loin and another in the suprapubic region. No organs were definitely palpable. The patient continued to get weaker and finally died rather suddenly April 18, 1925.

The Wassermann and urine examinations, blood counts and blood chemistry were negative.

Autopsy was performed twelve hours after death by Dr. Palomeque. The breast tumor grossly was as described in the physical examination. The mass was not attached to the underlying muscles except to a slight degree in one area. The mass was firm and cut with resistance. It presented a white fibrous core with a more cellular character at its periphery which presented a mottling of reddish brown to dark red. Search was

made for axillary glands and only a very small one of a gray color and soft consistency was found. The right breast and axilla showed no gross lesions. On opening the abdomen the whole upper portion was filled with a large cyst lying over the viscera and firmly attached to them, but having no attachment to the pelvis. The cyst contained 1000 c.c. of dark cloudy fluid of 1.030 specific gravity. The uterus was grossly normal, but on either side the ovaries were replaced by large multilocular cysts, the largest being the size of a man's head. These cysts con-

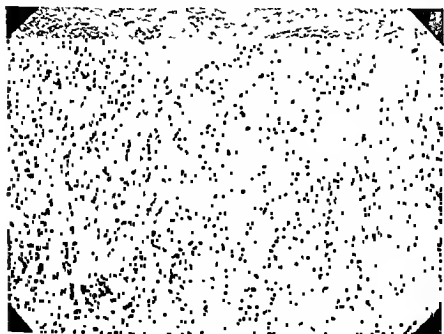


Fig. 51—Case 1 Medullary adenocarcinoma of the left breast

tained similar fluid to that in the upper abdomen. The cysts walls were lined with papillomatous overgrowths. Nearer the uterus on either side the masses were more solid, irregular in size and shape, and on section consisted of a grimy cellular tissue of the same nature as the papillomatous material lining the cysts. The ovarian tumors together with the uterus weighed 18 pounds. The stomach was normal in size. On both the anterior and posterior walls in the lower half of the stomach several pedunculated polypoid tumors of a soft consistency were found. These polyps grossly appeared benign.

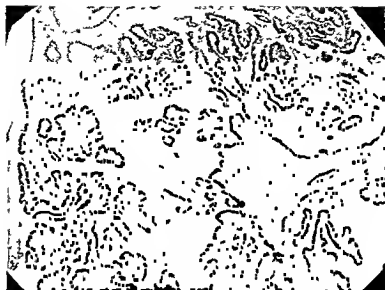


Fig 52 —Case 1 Papillary cyst adenocarcinoma of the ovary.



Fig 53 —Case 1 Adenoid carcinoma of the stomach

The microscopic section (Fig 51) shows large clumps of anaplastic cuboidal glandular cells atypical in size shape and arrangement. These cells can be seen penetrating irregularly into the deeper tissues. There is a great deal of fibrous stroma separating the clumps of cancer cells. The cells are not arranged in acini, but occur in cords and clumps. There is no lymphoid infiltration in reaction to the growth.

The microscopic section (Fig 52) shows a thick cystic wall and septa with papillary projections into large cystic spaces. The papillary projections are lined with atypical columnar cells which are heaped up in places and are of an anaplastic character. Within the spaces between the papillary outgrowths is a pink staining granular material of fibrinous and serous character. This is a typical microscopic picture of a papillary cyst adenocarcinoma of the ovary.

The microscopic section (Fig 53) is taken at the base of a polyp attached to the stomach mucosa. At the base of the polyp it is noted that there is an infiltration of moderately anaplastic cuboidal cells in glandular arrangement. This infiltration as will be noted, has extended fairly deeply into the muscle layers.

Case 2—R. H. a white woman sixty years old was admitted to the Philadelphia General Hospital April 1, 1925. Two years before death her right nipple became sore and soon began to bleed. Two months after onset the nipple sloughed off and three months later a lump appeared within the breast beneath the ulcerated nipple area. The lump became quite evident in a short time. An inflammatory reaction developed below the right breast nine months after the onset of the condition and hard rounded nodules could be felt in the skin around the tumor mass. No abdominal complaints were made.

Physical Examination—The nipple of the right breast is entirely replaced by a firm irregular, reddish brown crust. An irregular, firm nodule, fixed to the skin but not to the chest wall is palpable beneath the crust. No enlarged glands are palpable in the right axilla. The breast itself is atrophic and the skin

beneath it is inflamed and several subcutaneous nodules can be palpated. The nipple of the left breast is normally preserved, but an irregular movable nodule is palpable near the border of the sternum, but not fixed to either the sternum or the skin. No enlarged glands are present in the left axilla. The abdomen is distended, signs of free fluid are present, and many nodular irregular masses can be felt throughout the abdomen. Large thickened inguinal lymph-glands are present. The vulva and

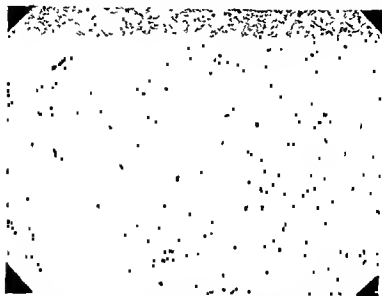


Fig. 54—Case 2 Medullary adenocarcinoma of the left breast

vagina are normal. The cervix is high and deflected to the right. The fundus and appendages are not made out.

Autopsy was performed sixteen hours after death by Dr. M. McCutcheon.

The right breast grossly was found as described in the physical examination. On section of the tumor a hard, gritty mass was found with a glistening white, hard fibrous stroma interspersed with small areas of yellow softer fat-like tissue. No axillary nodes were found, but small hard nodules were present in the left breast of the same character as the right. The liver and lungs

showed small nodules of the same consistency and character as the breast tumor. **Abdomen:** On opening the abdomen a slight amount of dense adhesions were present. Scattered over the parietal and visceral peritoneum were innumerable small papillary new growths 2 mm. in diameter and of the same character as the growth in the left ovary. The gastro-intestinal tract otherwise showed no abnormal changes. The uterus was atrophic. The left ovary was greatly enlarged and on section contained a soft cystic and papillary growth, the fluid contents

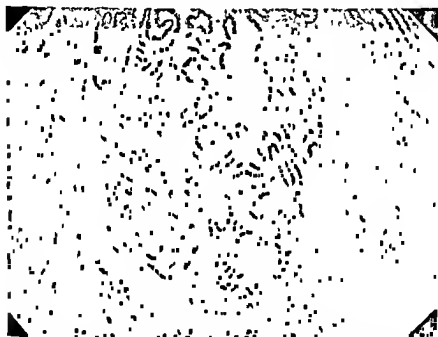


Fig 55—Case 2 Papillary cyst adenocarcinoma of the left ovary

of which resembled pus. The right ovary was atrophic but did not appear abnormal.

The microscopic picture (Fig. 54) shows clumps of anaplastic cuboidal epithelium simulating very closely the cancer of the breast in Case 1, except that there is more fibrous tissue in this. The liver and lungs show metastatic growths of the same microscopic character.

The microscopic section (Fig. 55) shows similar characteristics to the cystic cancer in Case 1, except that in this case the growth

is more solid and the cystic spaces small. The metastatic nodules on the visceral and parietal peritoneum show a similar microscopic picture to the ovarian tumor.

Comments—These two cases we feel are not only of pathologic interest but also of unusual clinical interest.

In the first case the ovarian tumor was the most important so far as symptoms were concerned, and played the largest part in causing the death of the patient. The tumor of the breast is an example of a great many cases arising from subinvolution or any benign tumor which remains benign for a long time and finally undergoes malignant change. It is quite evident that this tumor fifty eight years ago was benign and not of importance at that time. Just when this benign tumor underwent malignant change is very difficult to say but it as well as thousands of similar cases should be a warning to physicians and surgeons not to disregard insignificant small lumps, particularly in the breast when it is such an easy matter today to remove small tumors of this nature without any danger to the patient and submit them to gross and microscopic pathologic examination.

It was of great interest to us to have found occurring together with these two malignant neoplasms another example of an originally benign tumor undergoing malignant change. There were seven or eight of these polyps in the mucosa of the stomach and their grossly benign appearance is responsible for our not having taken more than one for microscopic study. We are thus unfortunately unable to say if any of the other polyps showed any malignant change. The microscopic description and photograph show quite plainly that this polyp is in an early stage of malignancy. In contrast with the first case the second patient's complaints were produced by the breast tumor and the ovarian cancer was of less importance symptomatically, although it had given rise to wide spread implantations and ascites. These cases make us wonder just what percentage of cancers begin as benign growths which either slowly or rapidly become malignant. There are a great many cases which we feel sure are malignant from the beginning. There are still a great many others we feel sure are benign in their early stage. A great many of apparently benign

tumors are removed by cautious surgeons and microscopically some of these show early malignant changes. These represent a class of originally benign tumors which for some reason rapidly become malignant. It is these cases that swell the roll of cancers cured by operation. Then there is a large group which pathologists consider benign but potentially malignant. These neoplasms possess a great many earmarks of malignancy but not enough to make a definite diagnosis. Various pathologists may differ as to the diagnosis of the tumors being benign. A great many of these cases, too, fortunately get well after early removal of the suspicious growth. Dr J. C. Bloodgood has said that neoplasms about which pathologists disagree as to their malignancy, if properly treated frequently are cured, while those cases which are definitely malignant to all pathologists usually kill the patient.

When a clinician or surgeon sees a case of the character of either of these unless he is aware of the occasional occurrence of multiple primary malignant neoplasms he will be at sea in attempting to explain a great many of the signs and symptoms. Then, too, it would be a pity to subject a patient to the expense and suffering of a major operation and a radical one, and find later he had overlooked a neoplasm which in the end is responsible for the patient's death. One like the second case could readily be an example of this nature.

The rarity of the occurrence of multiple cancer in one individual raises the question as to whether a malignant growth protects the individual against the occurrence of independent malignant growths. *It is obvious that no adequate protection is afforded against metastasis of the primary tumor (except possibly in some organs such as the spleen), but experimental cancer work has shown that in many cases a primary cancer even if excised early, will confer permanent protection against further transplants.* Some clinicians, on the other hand, believe that one cancer predisposes to another, but that the rarity of multiple cancers is explained by the early death of the patient from the primary growth.

These two cases might suggest this latter view to some extent.

The first case presents a breast tumor which had been present for fifty nine years and without a doubt has been benign until recently. The polyp of the stomach shows the very earliest malignant change, while the ovarian cancer had been present at least for two years when it gave rise to the patient's first complaints. These facts cause us to feel that it is possible for the ovarian malignancy to have had some influence on the two other previously benign tumors causing them to become malignant. The second case suggests similar lines of thought. In this case the breast tumor has in all probability been malignant two years. How long the ovarian cancer has been present is difficult to say. It at any rate had not caused the patient a great deal of trouble, although it had given rise to implantations and ascites. From other cases being studied we hope to throw light upon the subject, but at the present time the question of influence of one cancer upon other tissues must remain unsolved.

CLINIC OF DRS JAY FRANK SCHAMBERG
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RADIOLOGIC DEPARTMENT, PHILADELPHIA GENERAL HOSPITAL

RADIUM IN THE TREATMENT OF ANGIOMATA

THERE are various types of so called 'birthmarks' They are all characterized by a hypertrophy of one or another element of the dermic architecture It may be the blood vessels the pigment, the hair, the lymphatics the fibrous or epithelial structures At times a combination of hypertrophies exists as is seen in the "pigmentary and hairy mole" or the pigmentary and papillary or warty moles

There are also several varieties of blood vessel hypertrophy We may have a flat angioma or "port wine stain" Not infrequently there are observed circumscribed elevated lesions—"nevus angiomatosus" Thirdly, we may have extensive elevated deep seated blood vessel tumors—the so called "cavernous angioma"

While most nevi are present at birth some may develop at a later period

There is no satisfactory method of treating 'port wine stain' at the present day Occasionally one may obtain a fairly good result with strong ultraviolet treatments with compression lenses but the failures are far more numerous than the successes It is very doubtful whether radium in these cases lessens disfigurement

In raised angiomata on the other hand excellent results may be obtained by one of two methods In relatively circumscribed cases that are not accompanied by hypodermic bogginess and swelling we prefer the use of the solid carbon dioxide The ultimate cosmetic result is excellent, the condition often disappearing without any scar

For the very large or very deep cavernous angiomata radium is to be preferred. Likewise in the angiomata involving the lip and mucous membrane of the mouth it is superior to any other method. Radium emanation has given us excellent results in the cases treated in our clinic.

A brief report of these cases is herewith subjoined.

Case 1—C W Female aged six months. Was brought to the Radiologic Clinic on 3/4/25 with a huge cavernous angioma involving three quarters of the left ear and extending over the mastoid region, part of the cheek and below the ear to the



Fig 56—C W Female aged six months Photographed March 4 1925

neck. The tumor was about 10 by 8 cm elevated about 4 cm above the level of the skin (Fig 56). It was elastic to the touch and of a bluish red color. The patient received the following treatment. Three applications were given on 3/4/25 5/7/25, and 9/16/25, each of 1500 millicurie hours at 3 cm distance in a tray.

On January 12, 1926, Fig 57 was taken. An enormous improvement was evident. Two thirds of the growth has disappeared, and two thirds of the ear is now exposed to view and the normal contour of this part has been re established. At this time there was still angiomatous tissue over the lobule of the

ear and on the cheek anterior to this area. On April 7, 1926 improvement was still further evident. Anteriorly there was still some tumefaction, but none posteriorly. The external ear was normal. The patient is still under treatment.



Fig 57—C W Female. Same patient as Fig 56. Photographed January 12, 1926.

Case 2.—R G Female, aged seven weeks. At birth there was a bluish discoloration on the upper lip, which enlarged very rapidly after birth. At first examination there was seen a dark



Fig 58—R G Female, aged seven weeks. Photographed September 7, 1923.

blue, soft, cone-shaped, spongy mass, involving almost the entire upper lip and projecting out as far as the tip of the nose. The central portion of the lesion had a small opening over which a



Fig 59 —R G Female Same patient as Fig 58



Fig 60 —Same patient as Figs 58, 59 Photographed May 23, 1926

crust formed There was difficulty in suckling and the child was under weight

Treatment—On 9/26/23 the child was treated with silver tubes: thirty millicurie hours; cross-fire.

10/22/23: There were two areas of ulceration on the upper lip with a marked decrease in the size of the tumor, which was no longer discolored.

11/26/23: Regression of about one-half in size of lesion with corresponding improvement in color. Baby nursing better and gaining weight.

1/6/24: Lesion almost normal in size except in the center and in the border. Further treatment nineteen and six-tenths millicurie hours to junction of mucous membrane and skin border of lip

7/31/25: No evidence of growth present.

Case 3.—J. W. Male, aged fourteen months The patient first came to the clinic on 1/15/23 He presented a bluish-red bulbous swelling of the nose, which gave him a most grotesque



Fig 61—On admission January 15, 1923



Fig 62—J W Aged fourteen months Photographed January 15, 1923

appearance (Figs 61, 64) The condition, according to the mother's statement, had its origin at birth in three purplish veins which gradually increased in size. Whenever the baby cried the nose swelled On examination, a cavernous angioma 1 inch in diameter was observed: it protruded $\frac{3}{4}$ inch from the tip of the nose.



Fig 63



Fig 64

Figs 63 64—Same patient as in Figs 61 62

The patient received seven treatments of forty millicurie hours, silver tubes cross fire at end of nose

On 9/22/24 the patient was vastly improved

Case 4—T J Male aged eighteen months The patient was brought to the clinic on 9 22 24 with a large angioma of



Fig 65—T J Male aged eighteen months

the lower lip, buccal mucosa, pillars, and tongue. The condition was present at birth, but had increased in size since. The treatment received was as follows:

10/23/24: $\frac{1}{2}$ mm. silver and 1 mm. aluminum, one hundred and fifty millicurie hours

1/9/25: $\frac{1}{2}$ mm. silver, one hundred and twenty-five millicurie hours.

5/19/25: Tray fifteen hundred millicurie hours.

8/12/25: Tray fifteen hundred millicurie hours.

11/1/25: Brass capsule two hundred and sixteen millicurie hours.



Fig. 66—T. J. Same patient as Fig. 65. Photographed May 23, 1926

By October, 1924 there was considerable improvement. The patient was seen in December, 1924, when the lip tumor had regressed considerably.

The patient is still under treatment.

Summary—Discussion.—We have treated 20 cases in all, many of whom are still under our care. The results in general have been highly satisfactory, in some cases brilliant. It is most gratifying to be in the possession of a remedial agent that

is able to improve or cure these deformities so physically disfiguring to the patient and so distressing to the parents

As a result of our experience we would suggest the following thoughts

1 *Flat Superficial Angiomata or 'Port Wine Stains'* —The results in this type of angioma are very unsatisfactory. A slight to partial fading is the usual outcome in those cases that respond at all. Extreme caution must be observed in the application of radium to this type of lesion. Too heavy dosage will produce uneven fading, scarring and possible telangiectasis. Small areas may be treated with a light filter such as a $\frac{1}{2}$ mm. of aluminum giving 25 per cent. of an erythema dose every other day for three or four applications. No further treatment should be considered within eight weeks. We think it is a good rule not to repeat a radium treatment of any angioma for six to eight weeks after the time one thinks another application would be beneficial. This statement is made because we have observed improvement continue many weeks after the maximum effect of the radium has ordinarily been obtained which is usually six to eight weeks following treatment especially when one is working with a marked suberythema dosage.

2 We have treated one case of a slightly *elevated angioma* the surface of which was very irregular and studded with minute *papillomatous* vegetations. In this patient we employed $\frac{1}{2}$ mm. of silver as the filter and gave three quarters of a total erythema dose at contact in two applications forty eight hours apart. The dosage necessary to produce an erythema with $\frac{1}{2}$ mm. of silver at contact is twenty two millicurie hours.

3 In the next group we include the *raised angiomata* and the *submucous* and *subcutaneous tumors*.

For the small raised lesion which is very superficial in character we use one, rarely two silver tubes at contact with the skin and give a dose just short of an erythema. The result is very satisfactory. This type of angioma may likewise be most satisfactorily treated with solid carbon dioxide.

In the larger more extensive angiomata gamma radiation has given us by far the best results. We use a pack 24 c c in

area, filtered by a wall of 2 mm. of brass, in addition to $\frac{1}{2}$ mm. of silver in which the radon tubes are enclosed. The latter are placed in slots in the brass tray and arranged so that the radiation is evenly distributed over the entire applicator. This is placed over the angioma at a distance of 3 cm. The dosage we use is twelve to fourteen hundred millicurie hours, the erythema dose with this applicator being twenty-two hundred millicurie hours. A repetition of the treatment is never made within eight weeks at the very earliest, and we recommend an interval up to four months if the tumor is responding satisfactorily.

For deep-seated angiomata, or those of a comparatively superficial character but presenting difficulties in applying the radium, such as those involving tonsil and pharynx, we use a larger pack at 6 cm. distance from the skin, and give 25 per cent. of the total erythema dose of this applicator, the latter being twelve thousand millicurie hours. This dosage is repeated every six to twelve weeks, according as the lesion does or does not respond.

The few cases of *lymphangioma* we have had have been treated in the same manner, but the results have not been nearly as satisfactory as with the angiomata.

As a general statement we believe that the type of radiation depends upon the character of the angioma. Good results are dependent upon proper filtration and distance of the radium. For instance, a filtration allowing soft radiation to pass through will not alleviate a large, bulky tumor. On the other hand, it is unnecessary to employ a hard gamma ray in the treatment of superficial lesions.

The utmost patience must be exerted: radium applications must not be hurried and the dosage must be held down. One must not expect to rid a patient of a large tumor within two years.

As a rule, the younger the individual, the better the final prognosis. Our best results have been obtained in infants four to ten weeks old.



CLINIC OF DR. JAY FRANK SCHAMBERG

PHILADELPHIA GENERAL HOSPITAL

BASAL-CELL CARCINOMA OF THE FACE

I DESIRE to exhibit a case of basal-cell carcinoma of the face which we have treated with radium with a result which, as regards cosmetic effect and freedom from recurrence, has been most satisfactory. This man is seventy years of age and suffered for some years with a large elevated, crusted patch on the side of the face. He had also a keratotic patch on one arm, which was treated in the same manner with radium. Both of these areas are completely healed and with very little scarring considering the extent of the original growth. I would not say that a similar result could not have been achieved by other methods of treatment, but the treatment with radium has been highly satisfactory and the patient has been free of recurrence now for a period of two years.

Much has been written in the past as to differentiation between prickle-cell and basal-cell carcinoma of the skin. The distinction, both with respect to diagnosis and prognosis, has probably been too definitely stated. There are occasionally basal-cell cancers which metastasize, and, on the other hand, most of the prickle-cell cancers do not. In general terms, the prickle-cell carcinoma is the more malignant of the two, but it should be realized that carcinoma of the skin of the face rarely gives rise to metastases; indeed, in an experience covering many years and some thousands of cases, I can count the cases which metastasized on the fingers of one hand. One of those which did give rise to a lymphatic metastasis was an insignificant-looking nodular growth on the lower eyelid. Some writers are casting doubt on the determination of malignancy of a growth as influenced by its prickle-cell or basal-cell character. Indeed, some

of the growths are mixed basal cell and prickle-cell carcinomata. Perhaps there is more truth in the statement of Broders of the Mayo Clinic that malignancy is determined by the degree of differentiation of the cell structure.

Of course the above statements as to the relative benignancy of cancer of the skin of the face do not apply to those affecting the mucous membrane of the lip. Here the tendency to lymphatic metastases is extremely great and early and thorough treatment is absolutely essential. Much has been said from time to time concerning the liability of *pigmented moles* to undergo malignant change and warnings have been given concerning the treatment of these cases. We have destroyed a very large number of pigmented moles over the course of many years with the happiest of results. So long as the entire growth is destroyed it matters perhaps little what means are employed. We have found however that adequate destruction can be accomplished by means of the thermocautery with very little scarring which is an important desideratum with moles on the face. To be sure electrodesiccation or excision may be employed but in our experience we have been able to secure a better cosmetic result with the thermocautery. In not a single case do I recall any malignant change to have followed the destruction. Perhaps some distinction should be made between the brown mole and those which are black. The latter perhaps have a greater malignant potentiality and should be destroyed with particular thoroughness.

Dermatologists have an opportunity to observe the course and the clinical causes of cancer of the skin and these are of interest in their bearing on cancer elsewhere. We find that excessive exposure to sunlight is a cause of cancer of the skin. Sailors and farmers are more subject to cancer of the face than those in other occupations. Colored people particularly the pure racial types rarely have cancer of the skin of the face. In a large experience I have only seen one case in a light colored mulatto. A very remarkable disease known as *xeroderma pigmentosum* occurs in groups of children in the same family, the children exhibiting a hypersensibility to the action of the

sun's rays and developing cancer as a rule before the age of five is reached. The condition is not hereditary, but there is a history of consanguinity in the parents in a considerable proportion of the cases recorded. The chemical action of crude coal-tar and crude paraffin is responsible for some cases of cancer of the skin. In white rats cancer may be developed experimentally by repeated painting with crude coal-tar. Cancers develop at times from the long-continued ingestion of arsenic. Not infrequently arsenic is prescribed for a patient with psoriasis or some similar condition, and the patient finds that it is cheaper and easier to medicate himself and he continues to take Fowler's solution over a period of years. These patients often develop arsenical keratoses of the palms and soles, and occasionally skin cancers elsewhere.

All of the causes enumerated bespeak some form of cell irritation, and from a clinical standpoint point against the parasitic view of the origin of cancer. Nevertheless, the possibility of the germ origin of cancer cannot be definitely brushed aside.

CLINIC OF DR EUGENE P PENDERGRASS

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EPIDERMOID CARCINOMA (EPITHELIOMA) OF THE LIP. THE DIAGNOSIS, PATHOLOGY, AND DISCUSSION OF THE TREATMENT BY NON-SURGICAL MEASURES

Terminology —Ewing¹ rightly suggests epidermoid carcinoma as a better term than epithelioma

Definition —Epidermoid carcinoma (epithelioma) of the lip is a malignant tumor or growth arising chiefly from the epithelium lining the skin or mucous membrane or both

Normal Histology ²—"Every mucous membrane comprises two distinct parts the epithelium, which forms the immediate free surface and protects the delicate subjacent structures and the tunica propria, a connective tissue stroma which gives place and support to the terminal branches of the blood vessels and nerves and the beginning of the lymph channels. A stratum of submucous tissue, ordinarily loose and extensible, usually connects the mucous membrane with surrounding structures.' In view of the frequency of epithelioma of the lip it seems advisable to call attention again to the fact that¹ "The histologic transition from the skin covering the exterior of the lips to the oral mucous membrane takes place gradually the two being connected by a broad intermediate zone which approximately corresponds to the red area of the lips. The oral mucous membrane is covered with stratified squamous epithelium 2 to 4 mm in thickness. The tunica propria consists of closely felted bundles of fibrous tissue and elastic fibers and passes into the submucous stratum without sharp demarcation. The subepithelial border of the tunica propria is beset with innumerable minute elevations, the papillae.'

The blood vessels lymphatics, and nerve twigs supplying the lips are numerous and the larger radicals are found within the submucous layer

Anatomy³—The upper and lower lips receive their blood supply from the facial artery on either side the branches of the two anastomizing very freely

Lower lip The inferior labial artery
The inferior coronary artery
Upper lip The superior coronary artery

The lymph vessels draining the upper and lower lips follow the courses of the blood vessels and drain into lymph glands (Fig 67) The lymph channels on each side communicate freely

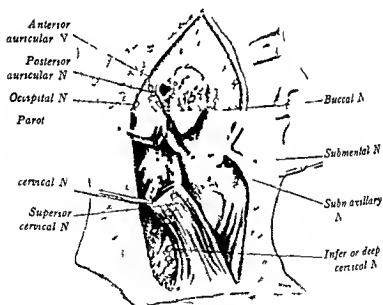


Fig 67—Illustrating lymph nodes in the neck draining the upper and lower lips

and are divided into superficial and deep layers The channels draining the lower lip drain into nodes which are divided as follows

Superficial	Submental glands
	Submaxillary glands
	Superficial cervical nodes
Deep	Submaxillary glands
	Superior deep cervical glands

The lymph-channels draining the upper lip drain into nodes which are divided in the following manner:

Superficial	Buccal gland
	Mandibular gland
	Submaxillary glands
	Superficial cervical glands
Deep	Submaxillary glands
	Superior deep cervical glands

There is free communication of the lymph-channels to both sides of the neck.

The sensory nerve supply of the upper and lower lips is derived from the second and third divisions of the trigeminal nerve. The motor nerve supply is derived from the facial nerve.

Pathology.—"Epidermoid carcinoma (epithelioma¹) of the lip is divided into two main groups; one group presenting flat squamous cells and sometimes called acanthoma and those presenting smaller cells of the basal type, and called basal cell carcinoma."

"These terms¹ may give a false inference that the one tumor is derived from the squamous cells of the Malpighian layer, the other from the basal cells. Yet acanthoma arises from the downgrowth of both basal and overlapping cells, which immediately exhibit some of the normal changes into flat cells, often with intercellular spines. Basal-cell carcinoma arises perhaps exclusively from the basal cells, often from misplaced and embryonal groups of such cells but the normal transformation into squamous cells entirely fails."

"Many subvarieties¹ of epidermoid carcinoma are observed. Acanthoma presents adult flat epithelium with hornification, concentric groups of cells flattened by pressure (epithelial pearls) are often intercellular fibrils. The squamous cells may become more and more atypical producing cellular carcinomas of many

<i>Points of Origin</i>		<i>Per cent</i>
Upper lip	Right side	33 33
	Left side	53 33
	Middle	13 33
		<i>Per cent</i>
Lower lip	Right angle	0 18
	Right side of midline	38 64
	Midline	17 75
	Left side of midline	43 60
	Left angle	0 56

<i>Metastases</i>		<i>Per cent.</i>
Parotid nodes		0 95
Submaxillary gland		21 90
Superior deep cervical nodes		7 89
Submaxillary nodes		87 61
Submental nodes		24 76
External jugular nodes		63 15
Supraclavicular nodes		0 95
Anterior cervical nodes		21 04
Inferior deep cervical nodes		7 89
Lung		0 95
Penthracheobronchial nodes		1 90
Liver		0 95

The above analysis demonstrates, as well as one can wish, the areas that should be thoroughly investigated in studying or treating a given case (Figs 73, 74)

Formerly, we have been content with a pathologic report as to whether a lesion was carcinoma, sarcoma, or a similar larger grouping of tumors, but now the pathologist has greatly aided therapeutic efforts by giving reasonably accurate prognoses from thorough studies of the microscopic sections Broders^{4, 5, 6, 7, 8} in a series of excellent articles has clearly outlined a plan by which a pathologic prognosis might be made, and if such studies are made on biopsy sections, the proper treatment of the given case should be more accurately employed

Broders^{4, 5, 6, 7, 8} suggests grading malignancy on the basis of cell differentiation In a tumor in which all of the cells are differentiated, the tumor is benign and grows very slowly with little tendency to metastasize. In a tumor containing all

undifferentiated cells the tumor is very malignant and gives rise to rapid metastases. Broders emphasizes the process of differentiation as an index of the self-control or nature's protection against regeneration.

The grouping is as follows:



Fig 73—Male aged forty. Had history of epidermoid carcinoma of lower lip removed by plaster. At time of his first consultation at this clinic he had a mass of enlarged glands and complained of pain in the neck and scapulothoracic region. An x ray examination of the neck seen above shows complete destruction of the body of the sixth cervical vertebra.

Grade I, Epidermoid Carcinoma. One in which differentiation of self-control ranges from almost 100 to 75 per cent, and undifferentiation from almost nothing to 25 per cent; that is, if three-fourths of the cell are differentiated and one fourth are undifferentiated, it is graded I (Fig 71).

Grade II, Epidermoid Carcinoma: One in which differentia-

tion or self control ranges from 75 to 50 per cent , and undifferentiation from 25 to 50 per cent (Figs 75-76)

Grade III Epidermoid Carcinoma One in which differentiation or self control ranges from 50 to 25 per cent , and undifferentiation from 50 to 75 per cent (Fig 77)



Fig 74—Same case as in Fig 73. An x ray examination of the sacro-iliac region showed destruction of both wings of the ilium near the sacro-iliac joint. These areas of metastasis are most unusual and so far as we can determine the first case of wide-spread metastasis on record. Unfortunately the illustration does not show the bone destruction as definitely as the original film.

Grade IV, Epidermoid Carcinoma One in which differentiation or self-control ranges from 25 per cent to practically nothing and undifferentiation from 75 per cent to practically 100 per cent (Figs 78 to 80)

Etiology—Epidermoid carcinoma of the lip is chiefly a disease of elderly men but is being recognized in an increasing number of younger men (Figs 81, 82). The cause is not known.



Fig 75



Fig 76

Fig 75—Male age sixty three Les on began following razor cut three years ago Never consulted physician until present time At present has lesion 3 cm in diameter with glands in the submaxillary region Les on treated locally by radium followed by surgical endothermy the following day Pathologic diagnosis Squamous epithelioma

Fig 76—Same patient two years after treatment He is perfectly well Lip scar is soft and there are no palpable glands in the neck



Fig 77—Male age fifty one Large epidermoid carcinoma of left lower lip No glandular involvement Patient did very well for six months Disappeared from observation for one year Returned at that time with considerable glandular involvement so much that no further treatment was recommended

For a long period of time cancer has been thought to be of infectious origin. Lately there is a tendency for the pendulum to swing toward the hereditary predisposition to cancer. Cohnheim's theory of cell rests is being rehashed. Whatever the actual cause, there are certain factors that must be recognized as predisposing causes and treated accordingly. Anything that



Fig 78



Fig 79

Fig 78 —Young man, age thirty-five. Lip injured during the filling of a tooth. It became swollen. Was treated by ointments for ten months. The appearance when he first presented himself for treatment at our clinic is seen above. The entire lower lip is involved and fixed to the underlying bone. Pathologic diagnosis: Squamous epithelioma. Wassermann negative.

Fig 79 —Lateral view of same patient seen in Fig 78, demonstrating the large glandular involvement in the neck. The glands are fixed to the jaw and quite tense. There is a tendency for the glands to break down.

tends to irritate or traumatize the lip, such as tobacco smoke and bad oral hygiene, are predisposing causes. Fissures of the lip, ulcers, chapped lips, or scratches are lesions in which epidermoid carcinoma sometimes develops. Some observers state that syphilis predisposes to carcinoma of the lip. Leukoplakia, keratoses, warts, papillomas, fissures, ulcers of over three weeks' duration, and pimples should all be recognized as potential



Fig 80—Same patient as seen in Fig 78 after treatment. The lower lip lesion was treated locally by radium and subsequently removed by surgical endothermy. No local recurrence developed. The glandular masses in the neck were treated by deep therapy and subsequently broke down. This has been the usual experience where there is a tendency for metastatic glands to break down deep therapy or radiation of any kind tends to aggravate the process and makes the patient more miserable than if nothing is done. Patient died six months after the treatment was instituted.



Fig 81



Fig 82

Fig 81—Boy age six. The youngest case of epidermoid carcinoma of the lip in our series. Patient had xeroderma pigmentosa. There is a history of consanguinity in the family. We also treated this boy's sister, age nine years, for epidermoid carcinoma of the face. The lesion involves the entire right lower lip and there are large lymph nodes in the submental and both submaxillary regions.

Fig 82—Appearance six months after radium treatment. The lip lesion is entirely healed. Glands in neck have largely disappeared.

precancerous conditions and treated accordingly (Figs 83, 84) Broders feels that it is not correct to call benign conditions potentially malignant when there is no proof that they will become malignant. It does not seem to me that such an attitude is a safe one and it is my opinion that the sooner the medical



Fig 83



Fig 84

Fig 83—Male, age fifty six. Patient is a farmer. Has a large epithelioma of the lower lip left side which is not well demonstrated in the photograph. The figure does demonstrate beautifully a coincident leukoplakia involving the entire lower lip and the patient gives a very definite history of the leukoplakia degenerating into an epithelioma. The entire lower lip was treated by radium and surgical endothermy. No recurrence in three years. Patient had submental metastasis before instituting treatment. The glands are still present and somewhat smaller. Pathologic diagnosis: Squamous epithelioma. Wassermann negative.

Fig 84—Male forty seven. Began as ulcer three years ago. Lesion involving entire lower lip. Probably developed from a generalized leukoplakia. Patient is a smoker. Pathologic report: Squamous epithelioma. Lesion removed by radium and surgical endothermy. Patient well today.

profession recognizes certain conditions as potentially malignant and suggests treatment and observation accordingly the better for the patient. Fewer patients will have to undergo mutilating operations if they are properly advised and treated for their so-called benign conditions.

Diagnosis.—Epidermoid carcinoma of the lip is easily recognizable, as are some of the precancerous lesions of the lip. It usually begins as a small indurated nodule, lump, or pimple. Oftentimes there is no ulceration at first if the lesion begins in one of the mucous glands. If it becomes superimposed upon a fissured lip or ulcer, there is a history of ulceration from the beginning. The ulceration tends to heal over by scabbing, and, if this scab formation is removed, another quickly reforms. Another history that one frequently receives is that the lip has scaled over a long period of time, the area subsequently becoming indurated, with a tendency to ooze a clear serum and to form a scab. This is usually the history where there has been a malignant degeneration of leukoplakia (Figs 83 to 86)



Fig 85



Fig 86

Fig 85—Male, age forty six. Lesion left lower lip. Present for five months before seeking medical aid. Lesion removed by surgical endothermy and radium. It has recurred four times since removal five years ago. Each recurrence treated as the first one. Patient has a peculiar type of mucous membrane, very granular everywhere, with multiple patches of leukoplakia. Has been kept under constant observation during the period of five years. This is the type of patient that we feel should always be watched and advised.

Fig 86—Same as Fig 85. Patient is well now, having had no recurrence for fifteen months. Patient is seen at intervals of three months. Submental glands are unchanged, still being easily palpable.

Some of the epidermoid carcinomas grow slowly, others more rapidly (Fig 84). Most of the patients, however, give a

history of several months duration before consultation with a doctor. Others give a history of having consulted a physician who prescribed a salve or applied a caustic and then dismissed the patient as cured or told the patient that the lesion was so simple as to require no further observation. Most of such patients permit the lesion to develop until metastases occur and it is too late to get the best results when they finally apply for treatment. No doctor should turn such a patient away without advising relatively frequent observations or suggesting the proper treatment.



Fig 87



Fig 88

Fig 87—Male age sixty two. This illustrates a typical epithelioma arising at the mucocutaneous margin of the right lower lip.

Fig 88—Male age forty four. Small epithelioma at left angle and upper lip. Patient had palpable submaxillary glands on left side. Lesion treated by radium and removed by surgical endothermy under general anesthesia.

The lesion may begin on the mucous membrane or on the skin surface, or it may begin where the two surfaces join each other. It may however occur in and affect any portion of the lip. In our series the majority of the lesions has been on the left side (Figs 87 to 92).

Epidermoid carcinoma of the lip is found more frequently in



Fig 89—Male, age forty three Large epidermoid carcinoma lower lip, with glands in submental and submaxillary regions Lesion treated locally by radium only because patient had a heart condition and subsequently disappeared from observation



Fig 90—Male, age fifty nine Lesion first noticed six weeks ago as a pimple Has grown rapidly Measurements $3\frac{1}{2} \times 2\frac{1}{2}$ cm Has a submental gland No submaxillary glands Lesion treated locally by radium and removed by surgical endothermy No local recurrence but two weeks after surgical endothermy nodes in right submaxillary region were very large These have increased in size in spite of deep therapy irradiation This patient illustrates the Grade IV type of epidermoid carcinoma with very little differentiation Treatment removed the local lesion but did not affect the glands End result poor

A lesion involving the lower lip usually metastasizes to the submental and submaxillary glands first and then to adjacent glands. When the lesion is on the upper lip the buccal, mandibular and submaxillary glands are usually involved first and then the metastases extend to the deeper glands of the neck.

Advanced epidermoid carcinoma of the lower lip tends to involve the bone of the lower jaw and when it does it becomes very difficult to treat. Epidermoid carcinoma of the upper lip



Fig. 95—Male age thirty-six. Case of granuloma pyogenicum. It is very confusing and has been mistaken for epithelioma of the lip by us until biopsy sections have been made.

especially when near the midline tends to involve the upper alveolus and extend up to and involve the areas of the face where the alae of the nose are attached. Lesions of this extent are very difficult to treat because the limits of the extension of the growth are almost impossible to determine. Cartilage one of nature's best barriers to carcinoma limits the growth in one direction but the lymph spaces in the loose tissues of the overlying skin furnish an excellent field for extension. Even after rather radical radiation and removal one often sees recurrences just external to the area of therapeutic endeavor.

The lesions that are most often confused with epidermoid carcinoma of the lip are the primary chancre of syphilis, tuberculosis and granuloma pyogenicum. Syphilis can usually be readily diagnosed by taking a smear for a dark field examination. Tuberculosis is readily recognized by microscopic examination of a smear. Granuloma pyogenicum is also due to an infectious organism usually a strain of *Staphylococcus aureus* (Fig. 95). The history of all these conditions should give one a very good idea about the diagnosis. A routine Wassermann should be made but a positive Wassermann does not necessarily mean that

lesion is syphilitic. There may be two conditions present. Granuloma pyogenicum usually occurs in young adults or children and has the appearance of granulation tissue.

In addition to the history, the most important aid in differential diagnosis is the biopsy. The specimens should be prepared by a relatively quick method, *i. e.*, the modified technic used in paraffin section work, in order that the slides may be studied at the end of forty eight hours. This prevents any delay and should be used routinely. The pathologist should be supplied with enough clinical data in order that the pathologic findings may be correlated with the clinical findings and a comprehensive conclusion reached. The biopsy will definitely differentiate the various lesions.

There are a number of clinicians who will possibly question the advisability of routine section because of the danger of setting up metastases by cutting into an actively growing lesion. We feel very strongly, however, that the risk taken in the removal of a small section for microscopic study is more than compensated by the added information, grading, prognosis and the correct diagnosis determined from a thorough pathologic examination.

In order that all risks of obtaining biopsy specimens be minimized, however, we advise the use of the endothermic scalpel. This allows one to remove any sized piece of tissue without losing any blood. The endothermic knife cuts the specimen very nicely, does not distort the pathologic appearance, and at the same time sears the cut surface and prevents bleeding. This should be and does seem to be a perfectly safe procedure.

To remove a section by the endotherm knife it is necessary to have good local anesthesia. For this we advise only topical application of a 10 or 20 per cent solution of cocaine, or some other local anesthetic. *If we do not feel that local anesthesia produced by hypodermic injection is a wise procedure.*

It has been clearly demonstrated that carcinoma extends by lymphatic permeation and occasionally by embolic metastasis. If one injects the field surrounding a growth it is not unlikely that the local anesthetic may be injected into a field of involved

lymphatics Theoretically when those tissues are ballooned out and diffused with a local anesthetic, some of the carcinoma in the lymphatic channels might be dislodged and sent to other portions of the body to set up metastasis *Local anesthetics applied topically are perfectly satisfactory*

History Record—One of the most important features in obtaining information in regard to epidermoid carcinoma is the permanent record We suggest the following record because it contains a questionnaire in regard to all lesions related to carcinoma of the lip or mouth In reviewing or studying a group of cases it is most discouraging to have to discard a number of cases because of insufficient data

RECORD FOR LIP AND MOUTH LESIONS

<i>Name</i>	<i>Age</i>	<i>Case No</i>
A Present illness	Date of onset	
	Contributing causes	Trauma
		Pipe smoking
		Tobacco chewing
		Dental plates
		Loose bridgework
		Sharp teeth
	Pain When	
	Where	
	Leukoplakia Location	
	Extent	
	Metastatic glands Location	
	Onset	
	Date of first consultation	
	Advice received	
	General condition	
	Date of recurrence	
B Past medical history	Chronic conditions	Lues
		Tuberculosis
		Diabetes
	Treatment	Ointments
		Hydrogen peroxid
		x Ray
		Radium
		Miscellaneous
	Operation	Date
		Surgeon
		Anesthesia

Removal Local
 Radical
 Excision Knife
 Endothermy
 Primary biopsy healing
 of wound Primary
 Secondary
 Type of incision

C Family history Prognosis
 Carcinoma
 Lues
 Tuberculosis

D Physical examination Weight Normal
 Present
 General condition
 Lesion Location
 Size
 Type
 Ulceration
 Induration
 Extension through cheek
 Teeth General condition
 Sharp
 Plates
 Poor bridgework
 Leukoplakia Location
 Extent
 Hypertrophied mucous membrane
 Operative scar
 Recurrence Location
 Extent
 Glandular metastases
 Submental R
 L
 Submaxillary R
 L
 Superior deep cervical R
 L
 Anterior cervical R
 L
 Posterior triangle R
 L
 Remote metastases
 Lungs or mediastinum
 Bones
 Distant organs or parts

E Remarks and laboratory findings

Treatment—General Discussion of Treatment *Local Application of Radium*—When superficial radiation is desired 50 mg of radium in $\frac{1}{2}$ mm aluminum capsules for filter should be the agent of choice. One half mm of aluminum screens out only 50 per cent of the beta radiation thus allowing 50 per cent of the beta rays for treatment. Theoretically the therapeutic rays are beta rays. When gamma rays alone are used they produce secondary beta rays wherever they are absorbed. Secondary beta rays are similar to primary beta rays.

Fifty mg of radium screened by $\frac{1}{2}$ mm of aluminum in contact with normal mucous membrane for one half hour will cause a decided redness and swelling of the tissues in ten days to two weeks. This condition is called radium reaction and will reach its height in about three or four weeks following which it will subside and probably disappear in six weeks (Figs 96-98).

The above dosage will cause the mucous membrane to blister. It is very important to advise the patient of this as otherwise he may feel that the lesion is getting worse and possibly change doctors. This may result in the patient going to a physician who on account of being unfamiliar with the treatment already carried out may give him advice for which under other circumstances there would be no excuse.

The radium reaction will also cause considerable pain which disappears when the reaction subsides.

It usually takes six weeks for the radium reaction to disappear. Subsequent treatment therefore should not be considered until the end of six weeks to two months.

Occasionally one finds that no radium reaction occurs at the usual time and such cases should be carefully watched. Delayed reaction is the term applied to this condition and implies that no evidence of reaction is noted until six weeks to two months after the application of radium. A great deal of harm might be done if this condition is not considered in such cases before planning subsequent radiation.

When it is desired to get local effect without the usual radium reaction the use of 1 mm thickness of black rubber tubing placed over the aluminum capsules absorbs the secondary

radiation from the aluminum and lessens the resultant reaction considerably

When deep effect of radium is desired, $\frac{1}{2}$ mm of silver filter is suggested This filtration absorbs practically 80 per cent of



Fig 96



Fig 97

Fig 96 —Male, age fifty four Epidermoid carcinoma of six weeks' duration
 Wassermann negative Responded to radium applied locally

Fig 97 —Same as Fig 96 two weeks later during radium reaction



Fig 98 —Same as Figs 96 97 Lesion entirely well Patient well No
 recurrence at end of five years

the beta radiation Therefore, one can apply the radium for a longer period of time because of the decreased number of beta rays to give superficial reaction Fifty mg of radium, $\frac{1}{2}$ mm of silver, applied in contact for forty-five minutes will give a similar

reaction to that noted above. Thus one can see that to get deep gamma ray effect it is necessary to increase the time. Using the same factors, one can safely give a dose one and one half times as large with $\frac{1}{2}$ mm of silver filter, as compared to $\frac{1}{2}$ mm of aluminum. Here also one can use rubber tubing to lessen the superficial reaction.

Example

50 mg radium $\frac{1}{2}$ mm aluminum contact time 30 min Desired reaction
 50 mg radium $\frac{1}{2}$ mm silver contact time 45 min Desired reaction

In applying radium locally to a lesion it seems wise to use multiple portals in order that the radiation may be distributed uniformly and a cross firing effect obtained. This will insure sufficient radiation to take care of the actively growing periphery (Figs 99-100).



Fig 99



Fig 100

Fig 99 —Cross-section of one radium tube in position over the middle of a lesion and the irradiation in such a position.

Fig 100 —Cross section of two radium tubes over the same size lesion. Note the possible cross firing effect of irradiation in the middle of the lesion and how much better the actively growing periphery is irradiated.

Radium may be applied to an epidermoid carcinoma of the lip in several different ways.

(a) Radium tubes may be applied to several portals at intervals of $\frac{1}{2}$ cm using enough radium to *cover the lesion and 1 cm beyond the indurated edge*. The adjacent area should be protected by lead. The radium tubes may be applied by adhesive (Figs 101-103).

One very important feature in the treatment of the lower lip is the protection of surrounding parts of the face especially the upper lip. Irradiation of surrounding parts is unnecessary and due to careless



Fig. 101.—Epithelioma of lower lip before application of radium.



Fig. 102 —Same case as Fig. 101 after application of lead protection to surrounding normal tissue.

tion of such a condition can be easily obtained by covering the surrounding areas with lead and rubber tissue. The use of lead alone is not sufficient to preclude a secondary radiation reaction. The cases of radiation dermatitis complain of more pain from the normal tissues radiated than they do from the diseased areas.

(b) Another way of applying radium locally is by a dental wax mold. The wax can be readily molded after it has been heated to a point slightly above body temperature. An impression of the growth can then be made and the wax cooled by cold water. The radium can thus be satisfactorily placed around the lesion in small depressions made in the wax by a hot brass



Fig. 103—Same as Figs. 101-102. The radium tubes are now in position.

applicator. The mold can then be applied to the lesion after protection of surrounding parts as arranged in Figs. 104-107. Dental wax is unsatisfactory when the patient has no teeth because of the likelihood of the mold sliding or moving and the radium coming in contact with an uninvolved portion of the lip.

(c) Radium needle implantation into the local lesion is not recommended except following bipolar endothermy. This is a procedure that, theoretically at least, tends to dislodge actively growing cells and permit them to be carried to distant parts.

Two months should intervene before any thoughts of a second series of radium therapy are entertained. This gives a

EPIDERMOID CARCINOMA OF THE LIP

sufficient time for the radium reaction to disappear and the residual growth satisfactorily determined



Fig 104 — Before application



Fig 105 — After application of dental mold to lip



Fig 106 — Dental mold with lead protecting upper lip



Fig 107 — Dental mold lower lip and 1 inch lead and several layers of rubber tissue covering lead to protect the upper lip

Generally, in computing dosage for a given lesion we plan to give 60 mg hours to a square centimeter of growth in a small

lesion and 70 mg hours to a square centimeter of growth in a large lesion. The growth should be accurately measured and the dosage computed in this way. Example: Epidermoid carcinoma 1 cm wide and 14 cm long should receive the following dose: 1 cm long \times 1.5 cm wide \times 60 mg hours = 90 mg hours. If there is 100 mg of radium available the time would be obtained by the following equation:

$$\begin{array}{rcl}
 \text{mg} & \text{hrs} & \text{mg} & \text{hrs} & \text{min} \\
 100 & 90 & 60 & x & \\
 & 100x = 5400 & & & \\
 & x = 54 \text{ min} & & &
 \end{array}$$

The time then would be fifty four minutes.

Endothermy.—In all epidermoid carcinoma measuring at least 1 cm in diameter we feel that the treatment is not complete unless the lesion is removed by endothermy. There are several types of endothermy:

I Monopolar or Oudin current. It produces a desiccating effect on the tissues.

II Bipolar or D Arsonval current. This produces a coagulating effect on the tissues.

III Endotherm knife: an undamped current that produces a cutting effect on the tissues.

Endothermy should be an excellent agent in the removal of malignant growths and when combined with radiation we feel that the best results are obtainable (Figs 108-110).

Experimentally it has been shown that malignant cells are more susceptible to radiation when the temperature has been elevated. Due to this experimental fact, we began to use endothermy in conjunction with radiation. The endotherm knife is of only recent origin and it has greatly facilitated our efforts.

To use endothermy one must have good anesthesia. Here, again we would like to go on record as being opposed to local anesthesia on account of the reasons given above. If the patient cannot be given a general anesthesia, such as ether or gas we prefer nerve blocking by novocain at a distant point. If ether

anesthesia is used, one should be very careful to remove any ether, or ether-soaked garments or covers, and to dry the mouth out carefully, before undertaking the procedure in order that

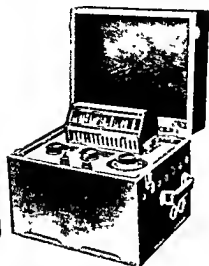


Fig 108.

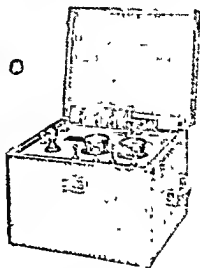


Fig 109

Fig 108—One of the machines used in supplying an undamped current for the endotherm scalpel

Fig 109—A compact machine used for unipolar or bipolar endothermy



Fig 110—Electrodes, hard rubber retractors, mouth gags, and equipment necessary for doing endothermy

no fire or explosion may take place. A window should be open to change the air. The patient is usually carried to a deep third stage anesthesia, and the work performed before the patient becomes conscious.

Rectal anesthesia is a most satisfactory one for this type of work especially when the operation is prolonged and radical. Otherwise the patient must be re-anesthetized sometimes as many as three times.

The type of endothermy used in epidermoid carcinoma is bipolar endothermy and the endotherm knife. The entire circumference of the lesion is coagulated the points of coagula-

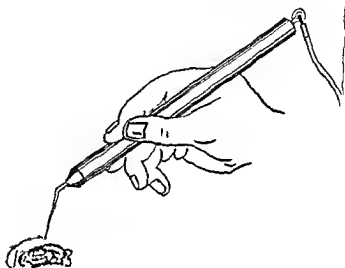


Fig. 111 —Illustration demonstrates the area of coagulation around the insertion of the needle and the procedure followed out in removal of such a lesion.

tion being $\frac{1}{2}$ cm. distal to the indurated edge of the lesion. A sharp needle electrode is preferable. The current is turned on and the needle is inserted into the tissue parallel to the base of the lesion and kept there until the immediate tissue around the needle is blanched. The electrode is then withdrawn and the entire circumference of the lesion covered in the same manner (Fig. 111).

It is very difficult to describe the type of spark necessary

Experience will teach one the spark to use in different kinds of tissue. Fatty tissue is more resistant than muscle tissue. As one's experience increases in the use of this agent, normal tissue can easily be differentiated from malignant tissue by the type of destruction produced.

It is not an infrequent experience, at the time of operation to find that the growth has infiltrated much beyond the limits determined by clinical examination. In this way we are able to supplement radium over the areas not treated prior to endothermy. This is usually done by radium needle implantation as at this time there is little or no danger of causing metastasis on account of the coagulation of the growth.

After the entire circumference of the lesion has been encircled by bipolar endothermy it can be removed in toto by the endotherm knife. In this instance also experience only can be depended upon to determine the best type of spark to use. Lesions can be removed in this way with scarcely any loss of blood (Figs 112, 113).

The patient will have no pain in the coagulated area until the slough begins to separate, because the nerve endings have been destroyed. When the slough does begin to separate in approximately seven days the patient will complain of some pain. There is also danger of secondary bleeding at this time and the patient should be advised accordingly. There is not enough danger of this however to deem it advisable to do a routine ligation of the external carotids. This in itself is a major procedure and necessitates manipulation in and around lymphatics of the neck, that may or may not be involved and tends to facilitate further metastases.

Endothermy is performed the day following radium application to the lip. We believe that such a procedure is best for the following reasons:

(a) We get heat plus irradiation therefore, theoretically, early endothermic removal following radiation is the procedure of choice.

(b) In a certain number of cases following radium irradiation glands develop in the neck in a location where no glands were

previously palpable. The reason for this we have never been able to fathom. Our thoughts, however, have been directed along the line of radium reaction. About ten days after the application of radium a severe reaction takes place evidenced by pain, swelling and engorgement of the tissues in the immediate



Fig 112



Fig 113

Fig 112 —Male age fifty nine. Les on began two years ago as a wart following a cut in a barber shop. Treated by a plaster expert for four months until he had no more money. At his first examination in our clinic the entire lower lip was involved and was firmly attached to the bone of the lower jaw. There were only two palpable submental glands. Wassermann negative. Pathologic report. Squamous epithelioma.

Fig 113 —Same patient as Fig 112. Les on of lower lip treated by radium applied locally and surgical endothermy. Deep therapy and radium over lymphatic channels draining area. The involved bone of the lower jaw was removed as a sequestrum. Lesion of lower lip entirely healed over year later. Only one small gland palpable. Patient still entirely well three and one half years after original treatment. The resulting scar from treatment is fairly well disguised by the overlying upper lip. No plastic surgery has been attempted.

vicinity of the treatment. That means an increased lymph and blood supply both of which would tend to carry along a loose malignant cell more easily than normally. Then too the lower lip is so situated that it is subjected to constant movement and trauma which also tends to dislodge cells easily. These thoughts

are our premise for possible permanent irradiation. If they are not, the irradiation is removed, the tumor

(c) The last case in the series was a patient who, 48 hours after radiation, had a decided recurrence of the tumor. The patient had a decided radium effect but the recurrence of the tumor is long-term.

The scar from our treatment was very close to the tumor. The patient was very comfortable. Radiation does not usually cause a recurrence. The patient is going out of the hospital and will be well covered. The patient may not be torn if the tumor is around the mouth.

For a local treatment, the patient is possible without causing a recurrence. When the patient is able, as well as the patient, how little discomfort.

Occasionally a recurrence of the tumor is endothermy. This is like a recurrence. When the patient is in which it tends to be a recurrence. The tumor is located at one or two places. It never involve the tumor. The patient should differentiate the tumor. It will remain here. It eventually without treatment.

When specific treatment is our opinion, the patient is simultaneously treated the other. In the malignant cells.

involved zone and create an endarteritis obliterans in the lymphatics and small blood vessels draining the involved area. In syphilis the treatment is directed toward breaking down connective-tissue barriers thereby eliminating the spirochetes into the blood stream and tissues where they can be more readily attacked by medication.

Our plan is first to irradiate the tissues until we feel that there has been a desired effect. Six months after the institution of radiation we believe it is safe to consider antispecific treat-



Fig. 114 —Portals of entry in treating glands in the neck and floor of the mouth by γ ray (10 inch machine). The arrows indicate the direction of the radiation.

ment. Generally speaking when the two conditions are associated the patient does not respond very well to therapy.

Irradiation of the lymphatics draining the involved area is accomplished by two methods.

γ Ray —If there is no glandular involvement or if there are a few small glands palpable γ ray is used. Irradiation (an erythema dose) is directed through each cheek toward the floor of the mouth (Figs. 114-115). The factors giving an erythema dose will of course vary with different machines and different altitudes. The erythema dose that we recommend is a slight redness approximately ten days after the treatment with slight

tanning at the end of four weeks. Erythema doses will vary in different individuals and in different seasons. In the summer time, for instance, one gets an erythema much more quickly than in the winter. Another feature that should be borne in mind in order to determine a safe erythema dose, is the fact that the neck is one of the most susceptible parts of the body to any kind of radiation.

It seems to me that the normal tissues surrounding an involved area play an important part in whether or not a given lesion will be benefited by irradiation. If it were possible to



Fig. 115 — See Fig. 114

determine the biologic factors concerned in the successful eradication of a given growth by irradiation, my estimation would be: Effect on growth itself by irradiation, 40 per cent, and effect on surrounding normal tissues, 60 per cent. If this premise be true, it would seem wise to preserve the normal protective functions of the surrounding tissues, rather than overirradiate them and destroy nature's barrier to the infiltrating growth.

For larger nodes, where there is no danger of the nodes breaking down, we prefer to use deep therapy irradiation. This is directed over each cervical region by carefully computed

dosage which depends entirely on the thickness of the part—the larger the neck, the larger the dose. The larynx should be well protected by lead, and overlapping of fields eliminated. The irradiation is given by fractional doses taking approximately two or three weeks to complete the treatment (Fig. 116).

Radium. In addition to the cross fire irradiation from the x ray, we have found by experience that it is advisable to irradiate around the chin covering the lymphatic channels draining into the submental and submaxillary nodes and also under the



Fig. 116—Portal of entry in deep therapy

chin and jaw over the glandular areas. These areas are not well adapted for irradiation by x ray. We have found that one can safely give an erythema dose of radium around the chin where there has been no x ray irradiation and one half of an erythema dose under the chin where there has been only stray x ray irradiation.

The type of radium applicator that we use for cross-fire irradiation over the lymph channels is a lead box mounted on flexible shaft in order that it may be adaptable to any part of the body (Figs. 11, 120).

An erythema dose by radium over normal skin can be obtained by the following factors

300 gm , 2 mm brass, 1 mm hard rubber, $\frac{1}{2}$ cm distance Time 30 min



Fig 117—Various radium applicators 1, Lead for protecting upper lip 2, dental wax mold 3, radium forceps 4, trocar for implantation of gold tubes 5 radium forceps 6, lead shield for epithelioma of lower lip, 7, radium forceps 8 dental wax before mold is made 9, radium filters (tubes of silver and aluminum) 10, radium forceps, 11, lead box (open) radium applicator 12, rubber tissue 13 flexible radium holder 14, card that is placed on bed of patient receiving treatment, 15, card placed on radium applicators

In irradiation of glands, or a local lesion it is wise to change filters if the desired effect is not obtained by the first type of filtration used. Anyone with any experience has noted time after time that a given lesion responded to aluminum filtration

when no effect was obtained from copper filtration. All growths are not alike, therefore one cannot expect them all to respond to the same treatment. We make it a practice to change our



Fig 118



Fig 119

Fig 118 — Illustrating the areas covered in cross fire irradiation by radium around the chin. When radium is to be applied to an area a diagonal line is drawn in the square. When the irradiation is completed another diagonal line is drawn from the opposite corners of the square thus making an X.

Fig 119 — Illustrating limit of areas under the chin.

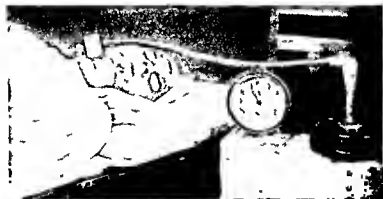


Fig 120 — Radium applicator in position

filtration if the desired effect is not obtained after the first treatment.

Irradiation over the lymphatic channels should not be repeated for at least six weeks after the completion of the first

series, in cases where there is little or no glandular involvement. When there is considerable glandular involvement, the interval between series should depend upon the result of the first treatment. A safe plan in determining the satisfactory interval for beginning a second series is to begin six weeks after the beginning of the first series.

Four series of x-ray and radium cross-fire irradiation seems to be a safe number to obtain a satisfactory result, if satisfactory results can be obtained.



Fig 121.

Fig. 121—Male, age sixty, with extensive epithelioma of the lower lip and glandular metastasis in the neck.



Fig 122.

Fig. 122.—Same case as Fig. 121 after application of radium and removal of lesion by bipolar endothermy.

In treating metastatic glands in the neck everyone is attempting to come to some conclusion as to which method of treatment is the best.

Primary block dissection of the glands of the neck is not advisable. In our experience these patients have been subjected to a mutilating operation with only an occasional good result.

Surgical exposure of the glands of the neck with subsequent implantation of radium needles, or emanation tubes, has been

of very little value. There are only a few cases living that have been subjected to this procedure (Figs 121-124).

Enlarged glands of the neck seem to respond to divided doses of deep therapy x ray irradiation or when possible, divided doses of gamma irradiation from radium. This is the conservative attitude and we vary the filtration if we do not succeed the first time. Some glands will disappear others will remain stationary or increase in size.



Fig 123



Fig 124

Fig 123—Same patient as Figs 121-122. The local lesion has entirely healed but the glands in the neck are still quite large. The neck glands have been treated by radium packs up to this time.

Fig 124—Same as Figs 121-123. The glands in the neck were exposed and emanation tubes (bare) were implanted into the glands and along channels of lymphatics. The patient continues in good health over a period of three years. The glands are barely palpable. There is no local recurrence.

If the nodes have been irradiated long enough to permit definite fibrosis to develop, and are gradually increasing in size, we advise the removal of the focus of malignancy by one of two methods:

(a) If the node is very large with some tendency to break down and is still movable we advise local excision of the enlarged gland without a wide block dissection.

(b) If the gland has not broken down we advise implantation of gold tubes containing 1.5 to 2 millicuries of radium emanation. The dosage should be approximately 60 to 75 millicurie hours to the cubic centimeter of diseased tissue. The gold emanation

tubes have sufficient filter to prevent the necrosis of tissue that formerly attended implantation of bare emanation tubes

In treating advanced epithelioma of the lower lip with wide-spread metastasis one can do very little to help the unfortunate individuals as far as eradicating the growth is concerned. However, there is a great deal that can be done to relieve the



Fig 125—Male age sixty one. Patient treated in another clinic, referred to our clinic for advisability of surgical relief of pain. Patient's lip lesion had disappeared but he had metastatic involvement of all the superficial and deep cervical glands on the right side of the neck. There were numerous sinuses draining pus and necrotic material. The patient had continuous pain that was requiring increasing doses of morphin to control. Alcoholic injection of the fifth nerve on the right side materially relieved the pain. Patient still had slight pain probably of cervical nerve origin but it did not seem severe enough to warrant rhizotomy of the posterior cervical roots.

excruciating pain from which they suffer. Through the excellent help and cooperation of Dr. Francis C. Grant⁹ of the Neurosurgical Department of the University Hospital and Dr. Temple Gray,^{10, 11} of the Neurological Department of the University Hospital, we have been able to offer the advanced cases entire comfort during the remainder of their lives. In some instances we have been able to get rather unexpected palliation. The

patient, relieved of the pain is able to sleep and eat and ceases to be a burden to his family. Psychologically, he feels much



Fig 126

Fig 126 —Patient had a subtotal avulsion of the posterior root of the fifth nerve



Fig 127

Fig 127 —The lines drawn on patient's face denote the limits of the anesthesia



Fig 128 —Areas of anesthesia in patient who had metastatic glands in neck. The black lines denote area of anesthesia

better and his resistance is therefore increased. Palliative radiation is given also, with excellent palliative results in some cases.



Fig 129 —Drawing of operation field for ligation and section of the posterior roots of the upper three cervical nerves



Fig 130



Fig 131

Fig 130 —Area of anesthesia in a case with metastatic glands in neck after cervical rhizotomy

Fig 131 —Posterior view of same patient as Fig 130 showing area of anesthesia posteriorly

The procedure for relief of pain depends entirely upon the location of the pain. The most frequent operation for relief of pain is section of the fifth nerve or cervical rhizotomy or both. Cervical rhizotomy consists in cutting the posterior roots of the cervical nerves as they emerge through the intervertebral foramina on the affected side (Figs 12 & 13).



Fig 137—Male, age sixty-five. E lower lip. Has submental and submandibular and surgical endothermy. Patheloma. No local recurrence but glanc in spite of every type of treatment rende treatment

carcinoma of middle of
Lesion removed by
Squamous epi
to a very large size
months after first
ref

In reviewing our cases we were
how to organize our data in order that
Status usually not worth the time
In a given series of cases treated in our
cases which were well studied from 1921 to 1925
consideration of the cases that
were treated of 1921 to 1925
in which the first case
that treat some value

to know
ue.

PERIOD 1921-1924

LOWER LIP 58

NECK GLANDS

Cases with no metastasis at time of treatment	33
Cases with development of metastasis after treatment	3
Cases with no development of metastasis after treatment	30
Cases with metastasis before institution of treatment	25
Disappearance of glands after institution of treatment	5
No increase in metastasis after institution of treatment	10 (Fig
Increase in metastasis after institution of treatment	10 132)

All but 3 of these cases are living 1 died one year after treatment and 2 died two years after treatment Three cases have not been traced but it is relatively certain that they are living and well

LOCAL LESION

No local recurrence	50
---------------------	----

Eight cases developed recurrences that disappeared after a second treatment

UPPER LIP 6

NECK GLANDS

Cases with no metastasis before treatment	4
Cases with no metastasis after treatment	4
Cases with metastasis before treatment	2
No increase in metastasis after treatment	1
Increase in metastasis after treatment	1 (Fig
No local recurrence after treatment	6 92)

Of these cases 4 are living and well 1 died one year after treatment was instituted and 1 was not traced but is probably well without recurrence

Finally, to preserve properly efficient records of the cases treated a satisfactory record chart must be kept We have found the following charts (Figs 133 134) most adequate for our requirements

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- 4 Broders A C Squamous cell Epithelioma of the Lip Jour Amer Med Assoc March 6 1920 pp 656 657
- 5 Ibid Cancer & Self Control Med Jour and Record February 4 1921

- 6 Broders A C The Grading of Carcinoma, Minnesota Medicine, pp 726-730, December 1925
- 7 Ibid Epithelioma of Cavities and Internal Organs of the Head and Neck Archives of Surgery, July, 1925 vol 11, pp 43-73
- 8 Ibid Carcinoma, Archives of Pathology, vol 2, No 3, September, 1926 pp 376-381
- 9 Grant, F C Suggestion for Relief for the Pain from Carcinoma of Mouth and Cheek Amer Surg 81 February, 1925, pp 494-498

HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

Reduction Therapy Record

Name _____

Case No.

Discussion

Radiation Treatment

[illegible]

X Ray Treatment

[illegible]

Fig 133 —Therapy chart

- 10 Fay, Temple Surgical Relief of Pain in Deep Carcinoma of Face and Neck, Amer Jour Roent, 14, July, 1925, pp 1-5
- 11 Fav, Temple Cervical Rhizotomy for Pain in Carcinoma of the Neck, Surg, Gyn, and Obst, September, 1926, pp 366-372

HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

Radium Treatment Record

Name	Diagnosis	Case No
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Location of Treatment	Date of Treatment
-----------------------	-------------------

Me or Mgm	Filtration	Time	No of portals
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The active end of the radium applicator must be applied to each portal. After each portal has been treated it should be crossed off and the applicator applied to the next one. The radium applicator should be kept absolutely over the portals on which it is applied and not be allowed to overlap others. If it does overlap, it should be reported to the resident roentgenologist.

Doctor's signature _____

This treatment has been carried out as ordered

Nurse's signature _____

Notes by Doctor (describe details of treatment)

Nurse's record of treatment

Portals	Time applied	Time removed
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FIG. 134 —Therapy chart.

CLINIC OF DRS. ROBERT A. BRADLEY AND
PAUL O. SNOKE

RADIOLOGIC DEPARTMENT, PHILADELPHIA GENERAL HOSPITAL

THE TREATMENT OF AN ADVANCED CARCINOMA OF
THE SKIN OF THE FACE WITH RADIUM¹

RADIUM is of very definite value in the treatment of epithelioma of the skin, even in cases presenting a rather hopeless prospect, as the following case report will reveal:

M. R., an Italian woman, aged sixty-nine, was admitted to the Radium Clinic of the Philadelphia General Hospital October



Fig. 135 —On admission October 29, 1924.

29, 1924. She had a large, ulcerating mass involving the lip, nose, and left cheek adjacent to the nose (Fig. 135).

She had a small pimple on her face in close proximity to the left ala of nose, which she noticed during 1912. Two years

¹ This case is reported through the courtesy of Dr. Jay F. Schamberg from his service in the Radium Clinic of the Philadelphia General Hospital.



Fig 136 —Note d ffuse prickly cell invasion at lower edge of sect on also pearl format on



Fig 137



Fig 138

Fig 137 —Improvement after first treatment December 26 1924

Fig 138 —Small areas below eye before treatment February 6 1925

later it became larger and somewhat inflamed. No treatment of any consequence was attempted or sought for until 1922 at which time the growth had progressed to the size of a twenty cent piece and ulceration had occurred. Plasters and herb applications failed to help it. She was advised to have it removed surgically, but refused. During the following two years which brings her up to the time of admittance to this clinic the growth progressed rapidly.



Fig 139

Fig 139—Patient free of disease October 14 1926



Fig 140

Fig 140—Cotton in nostril improves cosmetic result

Examination on admission revealed that the left ala of the nose, 2.5 cm. of the middle of upper lip, and the adjacent portion of the hard palate have been destroyed. The edges of the area are inflamed, necrotic, and hemorrhage upon the least injury. The neoplastic process extends upward almost to the inner canthus of the left eye. A cauliflower like mass obstructs and protrudes from the left nostril. No regional lymphatic metastasis is present.

A clinical diagnosis of basocellular carcinoma was made but the biopsy examination showed the growth to be of the prickle cell type (Fig 136) Radiographs of the antra revealed them to be free of disease

Treatment On November 11 1924 four tubes each containing 120 millicuries of radium emanation filtered with $\frac{1}{2}$ mm of silver and 2 mm of rubber were applied 1 cm apart for one hour The usual radium reaction took effect (Fig 137) and in eight weeks the lesion was entirely healed except for a small area in the region of the inner canthus (Fig 138) This was treated with good results During March 1926 a recurrence on the anterior edge of the hard palate was radiated as were small areas on the inferior turbinate and on the nasal septum These have healed and the entire region is under control no obvious growth now being visible (Figs 139 140)

CLINIC OF DR G M DORRANCE

RADIOLOGIC DEPARTMENT, PHILADELPHIA GENERAL HOSPITAL

MALIGNANCY OF THE MOUTH

In this series of clinics the patients will be presented whenever possible. When this cannot be done I will point out in the histories of the cases the points which are worthy of note.

In malignancies of the mouth the important factors which must be considered are 1, The location of the lesion, 2, the pathologic report of the biopsy, and 3, the prevention of the extension of the disease to the lymphatic glands.

In this clinic, as in most city clinics, the cases have usually been treated elsewhere before coming under our care. Only too frequently this means that metastasis has already occurred. While these late cases increase our mortality, it affords us an opportunity to study the results of the many methods of treatment.

A distressingly large group of these patients subject their most valuable asset, life, to any sort of treatment offered. They place the opinion of the cheap charlatan or ordinary housewife in the same category as the expert.

Case 1 —The first patient I wish to present to you is suffering from an epithelioma of the lip. As you will note, the growth is large and involves one third of the lip. This patient gives a history of having first noticed a small abrasion about six months ago. This abrasion bled from time to time and showed no tendency to heal. Then it suddenly began to grow rapidly. He gives his age as forty three years but you will note he appears more like a man of fifty years. His past medical history is negative. Examination reveals normal physical findings with

a few exceptions. He has a foul, dirty mouth with many necrosed teeth. He has a moderate degree of anemia, a normal kidney function, and a negative Wassermann. He is approximately 40 pounds under weight—his present weight being 130 pounds.

Local examination shows the area to be well circumscribed. The glands of the neck are palpable. I would like to draw your attention to the method of examination for enlarged glands of the neck. Place the finger of one hand in the mouth and the finger of the other hand on the neck. You will find it very easy



Fig. 141 —Bimanual examination of the neck

to outline the submaxillary glands and other structures of the neck by this method. If anyone is interested, come down and try it. I would be very glad to have each of you demonstrate the virtue of this method. We think this bimanual method very much superior to the ordinary method of palpating the external surface alone.

Here is a case that to all intents and purposes is a localized lesion of the lip with a few cervical nodules. We think it is a case of prickle-cell carcinoma. What is the treatment of such a

lesion? We are more concerned with preventing the involvement of the cervical lymphatics than we are in destroying the local lesion

In a series of 33 cases of early malignancy of the lip most of which have been controlled by a biopsy only 1 has metastasized to the neck. This we attribute to our use of radium packs to the neck and radium treatment of the tumor, the details of which are described later

This is a much better showing than we have obtained by other methods. It does not mean, however, that radium and radium alone is the ideal for all lip cases

The next case is very similar to Case 1. Here you see the results of treatment

We have given external packs of radium to both sides of the neck for 12 000 millicurie hours, 6 cm distance, filtered with 1 mm of aluminum and 2 mm of brass. This will be repeated at a later time. There are two methods open for treatment of the local lesion in this case. First, radium alone, second, application of radium, and later removal of the entire mass by electrodesiccation. Desiccation was used in preference to electrocoagulation in this case since it gives us less scar tissue. Radium was applied to the lip and one week later a biopsy was performed. The area was then desiccated so that the slough would extend well beyond any possible tumor cells. Both the clinical and pathological diagnosis were prickle-cell carcinoma. You will note that the lip lesion has entirely cleared up, there is very little deformity, the cervical glands which were palpable are now harder, and have not extended

A word about biopsy. In this clinic it is the rule to have a photograph, a biopsy, and a follow up. While many decry the biopsy as unnecessary and feel it aids in causing metastasis by opening the lymph channels, I am insisting on it in all cases. The production of metastasis by removal of tissue is I think, entirely hypothetical and I have not seen any unfavorable results from the removal. As a matter of fact, the individual has a right to know what his disease is. The anxiety on the part of the patient suffering from a supposed malignancy is very great

and if the result is positive one can proceed with radium etc with more confidence. The reverse however must be considered. When the pathologist returns a report that shows chronic inflammation it misleads one or a report of malignancy where none existed. I have no time for the pathologic report which states suspicious. The clinician must use a pathologic report with discretion and be sure of his pathologist. If the report does not fit in with the clinical picture take another biopsy.

A word about taking a biopsy. It must be from a typical portion of the lesion and sufficiently large to give a satisfactory section. Time after time on following out a report of chronic inflammation we have found that the biopsy was taken from the edge and not from the tumor itself. The biopsy is then a two edged sword and its removal should not be considered a minor affair as shown by the following case.

Case 2 —A patient in affluent circumstances was treated as a private patient in one of the best clinics in America. He has an ulcer of the right side of the upper lip. A biopsy was done and the report returned as malignant. He was treated by radium and electrocoagulation methods. He visited several clinics all of them referring back to the original clinic for the pathological report. They proceeded to give x rays etc until he came to Dr W. L. Clarke of this city. By this time he had lost his nose upper lip and had contractures of the face from x ray burns. Dr Clarke upon making a complete physical examination found a four plus Wassermann and other signs of syphilis. He was referred to me for plastic repair. This biopsy was certainly misleading and so I warn you against depending absolutely on a pathologic report. Many will say perhaps this man had both but from the history one would suspect a syphilitic lesion rather than a carcinoma.

Case 3 —The next case is one where radium pack to the lip and electrodesiccation treatment was carried out. No glands were palpable at the time of operation. At the present time the

patient is free from the disease and will have another radium pack to both sides of the neck. After our extensive experience we now feel that these patients have been under radiated rather than over radiated and it is wise to continue radium packs to the limit of skin endurance. We feel that we should continue these packs for at least one year. In that time we would complete approximately three erythema doses. I might add that we are not at all sure that complete x ray therapy to the neck does not give as much satisfaction as the radium, but we are limiting our treatment to radium at the present time and are satisfied it is giving us the best results we have obtained.

Case 4—The next case is one of malignancy of the lip. Twelve months ago the lip was removed by electrothermic methods. At that time the neck was said to be free from glandular involvement. As far as we have been able to determine no x ray or radium therapy was applied to the neck either before or after the primary removal of the growth. I would especially like to draw your attention to the fact that it is the prevention of the enlargement of the cervical glands which is the difficult problem, removal of the local lesion being comparatively easy, and with simple surgical excision alone we do not encounter local recurrence in over 25 per cent of the cases. With radium and the electrothermic methods the local recurrences are many times less. Glands were noted in the submental region six months after the original operation. They were treated by radium packs before he came to this clinic. You will note he now has no local recurrence of the lip but he has a hard, firm, fixed mass in the neck. By bimanual examination the mass is irregular, movable and from the history it is apparently not progressing. The pathologic report obtained from the surgeon who saw the original condition was epithelioma of the lip. This man has a great deal of pain in the neck and in the area of the mental branch of the inferior dental nerve. In seeking the cause of the pain we had the jaw x rayed and found it to be normal. What is the best method of treatment for this man? Since coming under our care he has had a full erythema pack of

radium to both sides of the neck. Two months have elapsed since this treatment. The mass in the neck is a little smaller and harder. It now needs more radium and I will introduce radium seeds around the margin and into the substance of the mass. Later on he will have more external packs. What is the prognosis in a case of this character? The original growth was eradicated completely and while we do not expect a local recurrence one must always be on guard for it. The glands of the neck are a very much more serious condition, and I do not expect this to disappear but do expect to keep them under control for approximately one year. We have not cured any cases with decided enlargement of the cervical glands and all of our cases with this complication have died within the second year limit.

Case 5—Recurrent Epithelioma of the Lip with a Few Scattered Enlarged Glands of the Neck—His lip was removed six months ago by the electrothermic method. No treatment was given to the neck. I desire to impress upon you that the prevention of neck involvement is the important point of the treatment. Note he has a recurrence of the lip. Electrothermic method alone perhaps was not radical enough. We would have used radium first and the neck would have been given a prophylactic treatment. Since coming to this clinic we have applied radium packs to the lesion and both sides of the neck and we will now electrodesiccate the entire local lesion. Certain of the cases of the scattered enlargement of the cervical glands cleared up very rapidly. They were undoubtedly not malignant. We have tried numerous methods to prevent the glands from becoming involved. The first of these was surgical removal under local anesthesia by block dissection. We opened all necks and removed all glands. Secondly, we performed a block dissection on all necks showing glands. I might add we soon found it better to remove only the structures below the submaxillary fossa at one sitting and later the remainder. Infection is prevented in this manner. As you will note in this case, I am not going to do a block dissection but depend upon radium packs. Recurrence after block dissection has

been the rule. We do not like to have the skin or mucous membrane broken if we are using radium. Another point to be considered is that the skin does not heal as well if large doses of radium are used. We have discontinued these methods, as we do not think them as satisfactory as radium therapy. As these growths most frequently occur in those well along in years, we find they do not stand operative treatment well. We have dissected the neck and introduced radium seeds after we have removed all glands possible. It is surprising when one does a block dissection of the neck to note how often glands are found which could not be palpated, and how frequently a careful microscopic examination reveals them to be malignant. We are becoming more convinced as time goes on that one should select one method of procedure and not attempt too many combinations of methods. One point is quite evident, if the skin is ulcerated these patients do very badly. This is also true when mixed infection occurs notwithstanding the feeling that some cases of malignancy are cured by very severe infections such as erysipelas. I have never seen a cure occur, but, on the other hand, I have seen many cases of malignancy do very badly after infection. Dr H. K. Pancoast and myself selected 14 cases to try radical dissection and implantation of radium seeds where it was impossible to remove all the malignant growth. In only 2 were we satisfied that the method had any value, and those had had external radiation. Where we used small amounts, the malignancy continued, and where we used large amounts, sloughing ensued. We discontinued the method. However, in selected cases we have dissected out the disease and implanted gold tubes.

In reviewing the cases which have presented themselves to this clinic suffering from malignancy of the lip, we find that local removal of the growth has usually been well performed regardless of the method employed. The method employed in the order of frequency has been surgical removal, coagulation or conglutination and radium pack or radium alone. Careful systematic treatment of the neck has been the exception rather than the rule, one or more courses of x ray being the usual treatment. While

we have been able to hold a number in check for a long period of time we feel that the time to prevent the lymphatic involvement is when the primary growth is first seen. Then treatment directed to the neck offers the most hope. This final case of epithelioma of the lip I will show you is one where the entire lip is destroyed by disease or numerous operations and where you will see both sides of the neck involved with large masses of glands. As the patient is an absolutely hopeless case I feel that no treatment except to relieve pain should be given. The radium will only increase his pain without being of any benefit to him. Small doses of x ray have at times given relief from pain. Multiple small doses of x ray by J D Morgan's technic have held many cases in check some have greatly improved.

We have attempted on several occasions to dissect these masses out under local anesthesia but have found the structures so matted together that only a partial removal could be performed. Our work was of no value and it only made the patient more uncomfortable.

Malignancy of the Buccal Mucosa—Before discussing these cases I would like to take up the question of leukoplakia of the mouth. Leukoplakia may arise anywhere in the mouth. It is found most commonly below the entrance of Stenson's duct. We encounter two varieties of whitish patches—smooth and rough patches. While it is most common in smokers it does occur in individuals who have never used tobacco. As malignancy frequently develops in the buccal mucosa from these patches and this is one of the predisposing causes of malignancy it is well for us to consider methods of removal. First and foremost the teeth of these individuals should be put in perfect condition. Smoking should be interdicted and the mouth washed with dilute peroxid which is apparently the best way of keeping it clean. If the area is localized as it frequently is to the inner surface of the cheek there are two ways to remove it. First by dissecting it out and second by destroying it by electrothermic methods. Having used both many times I am sure surgical removal is superior where the area is of limited size. The anesthesia necessary for the operation is obtained by

local injection of novocain and adrenalin. The fluid raises the mucous membrane so that it is easily undermined with a pair of scissors curved on the flat. After the leukoplakia patch is removed the surrounding mucous membrane is undermined and if the leukoplakia has been limited to an area the size of a quarter the freed mucous membrane can be sutured together. However we frequently destroy it by desiccation. I assume of course that the Wassermann is negative. This brings up the point that leukoplakia is more common among the patients having had syphilis. If leukoplakia recurs twice in one localized area it has been my experience that one should then be very radical in the removal of this area. I have seen cases of simple leukoplakia untreated after a lapse of several years go over to malignancy. While irregular teeth etc. may and undoubtedly have some effect upon producing malignancy it is a curious fact that the malignancy develops about the place where the cheek comes in contact with the upper and lower teeth. Traumatism, therefore, unquestionably plays a part in producing leukoplakia and assisting its progress to malignancy.

This present case presents a malignancy about the size of a quarter and involves the mucous membrane of the cheek. It started as a leukoplakia gradually the area became thickened and bled from time to time. From a clinical standpoint there is no doubt that it is one of the types where malignancy developed upon a leukoplakia. You will note that the skin is freely movable over the area and there is no glandular involvement of the neck. I would add here that these cases are slow to develop metastasis to the neck. The treatment in this case will be radium pack to both sides of the neck at once, this will be repeated several times during the coming year. He has already had radium pack to the cheek and I will now proceed to destroy all the inner surfaces of this cheek with the electrodeiccation method. As you will see I am able to remove all the diseased area without affecting the appearance of the skin. If I were not able to do so I would not for a moment hesitate to destroy the entire cheek rather than take any chances on the malignancy recurring. This case illustrates our method of procedure in all cases of this

type viz radium packs and removal of the entire area of the disease at one sitting

The next case has a most interesting history. He was treated for leukoplakia by radium packs. From his history it appears to have had no effect the growth continued to progress. He was then treated with serum at one of our pseudoscientific institutions. The cheek is now involved there is an opening into the mouth and he has bleeding from the sloughing area. In the first place radium does not have the desired effect upon leukoplakia. From my experience I would say it usually has a harmful effect so of course I do not use radium in leukoplakia. What are we going to do for the above case? Two weeks ago Dr McShane ligated both external carotids on account of a secondary hemorrhage. The patient has had almost continuous bleeding before this operation. The blood count has come up to 3 500 000 and hemoglobin 80 per cent. He is now getting small doses of x ray daily. Whether from the x ray or ligation the mass is decidedly smaller.

In a moderately advanced case as in the next case of prickle-cell carcinoma where the ulcer extends back from the left angle of the mouth $1\frac{1}{2}$ inches and the skin is involved but the neck glands are not palpable we give the radiation to the neck and then remove all the diseased area. This is best done by electrocoagulation methods. You will note how easily the entire area is removed in one mass by running the electrocoagulation needle through the entire cheek and using it as a knife. Now you will note the hole left in the cheek. The specimen removed will be studied to see if it corresponds with the biopsy of prickle-cell carcinoma. We will be able to close the defects in the cheek by plastic operations later. We feel it inadvisable to attempt to utilize the surrounding tissues for this work but by means of a tubed pedicle to bring in new tissue from a distant area. Observe this case. I removed almost the entire cheek eleven years ago. He had a malignancy similar to the one I have just shown you. This defect was closed with a pedicle flap. It is interesting to note how the skin which was turned in at that time has taken on all the characteristics of the mucous membrane with the

exception of the color. The color of the turned in flaps which has taken the place of the mucous membrane is snow white. I would particularly like to attract your attention to the fact that if you are going to eradicate the malignancy it should be done radically and widely. Do not let the fact that you will destroy the appearance of the cheek influence you for one moment because it is in these limited operations where the diseased area is not completely removed which give you recurrences.

Malignancy of the Floor of the Mouth — These are the most distressing types of cases we have. It is almost unbelievable that a man with a condition such as this man presents will tell you that he first noticed the condition some six weeks ago. As you will note he has an ulcerating area involving all of the floor of the mouth to the left of the tongue, greatly restricting the motions of the tongue. A biopsy of this showed it to be a prickle-cell type. There are no glands of the neck but the whole area is stiff as though it were infiltrated with gelatin. We are constantly imploring the public to come early to the clinic so that we can get them at an operable stage but in this clinic one is astounded by people reporting that they had not noticed ulcers in their mouths until they had gone over to the inoperable stage. I am doubtful of our propaganda for early treatment benefiting these mouth cases as most people do not seem to be able to recognize abnormal conditions in their mouths until it is too late to do anything for them. Malignancy when seen early in this area have not given us any cures from radical excision and very little more from electrocoagulation but when combined with radium the results are encouraging.

The patient I am about to present to you next is an excessive user of tobacco. He has a filthy mouth or, as I like to put it, 'he has a sewer all his own'. It is surprising to note just how filthy his mouth is and he seems to be unaware of it. Look at the tartar and debris around the roots of each of his teeth. Now it is rare for us to see small ulcerated areas of the floor of the mouth. This man, to my mind is practically hopeless in regard to cure. Before our treatment can be of any value his

neck will be infiltrated. However the treatment outlined for him is as follows. It is essential to clean up the mouth by the removal of all necrosed teeth, implant seeds or better gold tubes which we are now using. This is to be followed by radium packs to the neck to be given after the effects of the seeds have subsided. Then if he improves more implantation of radium seeds with two or more radium packs to the neck at various times depending upon the skin reaction.

Compare this to the next patient, a man seventy six years of age. He had an ulcer involving the floor of the mouth. Biopsy showed prickle cell carcinoma. His neck is free from glandular involvement. Five months ago he had radium seeds implanted in the growth and following this two erythema doses of radium given as packs to the neck. All that remains is a small thickened area about $\frac{1}{2}$ inch wide and 1 inch long in the floor of the mouth opposite the second molar tooth. We are not sure whether this is a recurrence or whether it is fibrous tissue following the use of the radium. However it seems to be getting slowly larger so we are going to implant gold tubes. We had better results from the radium implantation in our early cases than from any other treatment. We are more hopeful and much better satisfied with the results of radium therapy than from any other method we have tried. One should always remember that the electrocoagulation method is of great value. This class of case was formerly a very unfavorable type but with our present technic one can at least give a longer period from recurrence and we expect to be able to present some really worthwhile statistics in the future in this type of case. Time after time we have had patients present themselves to the clinic who have had surgical removal, electrothermic methods and recurrence has been the rule after all types of treatment. With the gold tubes now in use we are able to give a dose two or three times greater than when we were using the glass tubes. Prior to the use of gold tubes we were not at all optimistic about our results in the treatment of this type of case.

Late cases like the one which I present to you where the lesion started in the floor of the mouth and involved the tongue

and maxillary bone are absolutely hopeless if the neck glands are involved. He is having excessive pain because the inferior dental nerve is being pressed upon. We hope to inject alcohol into the third division of the fifth nerve to relieve this pain. We will take this up with you a little later. At this point I will take up the question of radium involvement of the bone. It is not as prevalent now as it was a few years ago when we failed to recognize the fact that destruction of the bone was produced by radium. When the radium comes in contact with the bone we are sure to develop this condition with its ensuing necrosis of the bone and its attending pain. Where this has occurred the only treatment I know of is to remove as much of the bone as possible—even to one half of the lower jaw if necessary. There are undoubtedly cases where on account of the excessive involvement it is necessary to implant radium seeds around the growth and take your chances of the bone being involved by the radium. Then, as soon as your malignancy is destroyed go ahead with the surgical removal of the bone tissue. A few years back I had 3 such cases with Dr W. L. Clarke where it was found necessary to give massive doses. These cases, which seemed absolutely hopeless were later cured by the use of radium, electrocoagulation and surgical removal of the dead bone—removal of the dead bone being my part of the treatment. These cases showed me very conclusively that a case involving the floor of the mouth, the side of the jaw, or even the buccal mucosa with the combination of radium plus wide electrothermic destruction, plus surgical removal of the entire half of the mandible, is decidedly worthwhile. In two of these cases it was necessary to remove one half of the lower jaw. I can report one of them free from recurrence after seven years, the second one was accidentally killed six years after operation, and the third one is, as far as I know, free from recurrence after a lapse of five years. In all three of these cases the defects were closed by plastic operations. I would again emphasize that if you are going to treat this type of case you should be very radical or not attempt to treat the patient at all. Malign frequently develops between the side of the tongue and th

type of tumor. They do not recur if the removal has been complete. No radium or x ray is necessary. It is then a tumor which usually springs from the membrane lining a tooth socket. This is the only tumor of the mouth where one can promise an absolute cure. I would caution against too radical surgery, as during the past year I have seen 2 cases where a section through the entire lower jaw was removed for this variety of tumor—an inexcusable piece of surgery. If the tumor was a sarcoma such surgery would not have effected a cure and for a giant-cell tumor local removal is all that is required. Both of the above cases required bone grafting to reunite the ends of the maxillary bone.

Another type of tumor is hypertrophy of the gums. I regret not to have a patient to illustrate this condition to you. This may be a localized growth surrounding one or two teeth but I have seen it involving the entire gum margins, both upper and lower. I do not know the etiology of this condition. They are of common occurrence in the young although I have seen them in patients of fifty three or more. The most successful treatment in our hands has been the complete surgical removal. From my past experience I would suggest that this be done in sections: i. e. remove the hypertrophy of the right side of the upper jaw then the opposite side then the right lower and then the left lower. As there is excessive bleeding to be expected from this area, I place a temporary clamp on both external carotids before attempting the removal. I have had no experience with radium for the removal of these hypertrophies but am perfectly satisfied with complete surgical removal.

Tumors of the Jaw—The tumor of the jaw in this case most likely originated in the antrum. The patient gives a history of pain in the right side of the face for months. Finally, the bones of the face seemed to increase in size and an x ray examination revealed bone growth. We removed almost the entire upper jaw by a combination of fulguration and surgery after first ligating the external carotids. As there was practically no bleeding at the time I worked very comfortably and no blood was lost. As you will see the entire jaw has been removed but there is still

involvement of the posterior lower part of what was the antrum. We have placed radium in this cavity, but on account of the late appearance of the disease we do not expect to control it. It is a sad fact that when most of these cases come to us it is too late to execute a complete removal with its attending results. However, Dr. Fielding O. Lewis has several antrum cases which he will undoubtedly show you. Instead of going in through the usual method in these cases, he uses the Crosby Green method of opening through the cheek and removing all the material possible. He then is able to apply the radium without the difficulty one encounters when going through the mouth.

This particular case shows that while the complete surgical removal of the entire jaw would be perfectly feasible, we have been content in removing all the anterior and lateral wall and are in a position to treat any local recurrence. At the present time, as I have said before, our standard treatment is a combination of surgery, electrothermy and radium treatment. My results have not been satisfactory, and while these cases do not metastasize early, they almost always recur.

Our next case is one of giant-cell tumor of the face. When I first saw her sixteen years ago she had all the characteristics of what was formerly known as the dog-face tumor. At that time I removed as much of the tumor as possible. Later I removed some more and this time I apparently removed most of it. Radium was applied nine years ago and since then we have been treating her with a ray of various dosages. I especially mention this type of tumor as it is amenable to radium or surgery. I now feel a combination gives one the best results. This is the type mentioned by Scudder in his book on tumors of the jaw which shows satisfactory results.

The next case is one of osteoma of the upper jaw involving the antrum and causing a deformity of the face. This woman, thirty-eight years of age, noticed a tumor gradually increasing in size and causing excessive pain. A Ray examination showed a solid tumor. The patient was a member of a doctor's family. A exploratory operation was performed. After ligating both external carotids we removed the osteoma with the greatest ease. I

might mention that this patient was previously treated by implantation of radium which caused an excessive amount of pain with no apparent change in the bone. We will close over the loss of the anterior wall of the antrum by a flap of mucous membrane from the cheek in this way doing away with that disagreeable symptom which she has of saliva flowing down her nose when she partakes of food or drink due of course to the parotid secretion from Stenson's duct flowing into the antrum.

Cysts of the Jaw—It is rare for a patient with a cyst to apply to this clinic for treatment as they are usually accidentally discovered when an x ray plate is taken. However we have several to show you today. The first one is a so-called apical root cyst. You will note a swelling beneath the upper lip and slightly to the right of the midline. The x ray plate clears up the diagnosis. You will note the right upper lateral is a devitalized tooth and there is a cyst involving the bone. This particular case will be cured by removal of the tooth and curing and packing the cavity. This procedure has been ordered. The next case presents the same symptoms with the exception that the swelling is in the roof of the mouth. Pressure on the growth causes a peculiar crackling noise like pressure on a ping pong ball. x Ray shows a cyst with an unerupted tooth in the sac. **Diagnosis** A follicular cyst.

The next case is one of a multilocular cyst. This condition was treated elsewhere. Removal was attempted but could not be accomplished because of hemorrhage. Two weeks later I ligated both external carotids and removed all the upper jaw with the exception of the floor of the orbit. You can see the ethmoidal as well as the posterior part of the septum of the nose. I think recurrence is inevitable. Dr. Pancoast tells me that x-ray treatment and radium have been of no avail in this type of case. Multilocular cysts of the lower jaw are more favorable than those of the upper jaw.

The next case is one of adamantoma of the lower jaw. We have had 3 of these cases on my service. We will only show 1 a man of fifty two years who was operated upon twelve years ago when the area was burned out, curetted and packed. Four

years later this procedure was repeated. Two years later I removed the entire left half of the jaw posterior to the incisor tooth and fulgurated the surrounding areas. It is now six years since he had his operation and we have him entirely well. We have no recurrence and the patient is wearing an artificial appliance. It shows very well that the loss of one half of the jaw does not greatly incapacitate an individual. The point to be borne in mind about these adamantomas in the lower jaw is that a very complete removal should be performed at the first operation. This is the golden opportunity for a cure. At the same time all the surrounding areas should be fulgurated. They recur locally and are very late in metastasizing. Radium and x ray have practically no effect upon them.

I wish to take up with you tumors of the neck. We have already discussed the secondary or metastatic gland involvement. It is quite a common occurrence for us to have patients present themselves complaining of a tumor of the neck. Upon searching the mouth one will usually find the primary lesion. These cases, of course, fall into the class of secondary involvement. However, there is a group of cases in which one has swelling along the anterior margin of the sternocleidomuscle approximately in its middle third without any primary lesion in the mouth or throat. We have had a number of cases and upon performing a block dissection and an exploratory to determine what the growth was the pathologic report has been returned—they were of brachyogenic origin. These cases are interesting only from a pathologic standpoint. When we have had the opportunity to see them it has been too late to remove the entire area. It is interesting to note that Dr. Pancoast states they are resistive to x ray and radium treatment. We have not been able to hold any of them in check. It is an interesting feature that the more you see of these cases and the further you search for the origin of the disease you will find small areas in the mouth particularly on the posterior surface of the tongue which had escaped your first inspection. In discussing this at one of the many conferences Dr. Carnett expressed my views very tersely when he said he was beginning to feel that all

of these cases were of secondary involvement where the primary growth had been overlooked and that undoubtedly while there was such a condition as primary brachio-genic malignancy it was very rare

Relief of Pain —There is one other phase of malignancy of the mouth I would like to take up with you and that is the prevention of pain I would call your attention to the fact that when you are considering the malignancy in these cases you must not forget the rest of the body In treating malignancy particularly of the mouth one must not forget the individual as a whole and fix one's attention on the jaw Particular stress should be laid on feeding as these patients are usually anemic It is surprising what one two or three transfusions will do in transferring them from poor to fair risks for further treatment While we do not believe that the starvation of the wound by cutting off the blood supply is of great value we do know that the ligation of the external carotid is a great help in preventing both primary and secondary hemorrhage While many are preaching removal of all foci in the mouth to prevent malignancy I do not think much is to be gained by this Patients come to us with the disease well advanced and state that they only noticed the condition two weeks ago While the crusade for clean mouths and removing leukoplakia patches are of great value from an asthetic standpoint up to the present time we have seen very little progress in the prevention of malignancy

As many of our cases come to us in the last stages of the disease suffering agonizing pain it has been a problem to devise ways and means to make their last days more comfortable

First let me go over the matter with you as we do in the Clinical Conference and determine the cause of the pain We have several cases where we can demonstrate the cause of the pain

Case 1 The original site of the cancer was on the lower lip This was treated elsewhere and he comes to us suffering excruciating pain from enlarged cervical glands He complains of

pain over the right mental nerve and in the region below the tongue. x Ray study shows the lower jaw to be normal. Examination shows the neck growth to be firmly attached to the lower jaw immediately below the mental foramen. He has been taking morphin which gives only temporary relief. Morphin is unsatisfactory as it interferes with the digestive tract, etc. They do not get sufficient nourishment while under its continued influence. We injected the third division of the fifth nerve with 90 per cent alcohol at the foramen ovale and produced anesthesia over the distribution of the nerve. Under local anesthesia we exposed the second and third cervical nerves and divided the sensory branches causing loss of sensation over the right upper half of the neck. This has been a most successful procedure in this case. He now eats with comfort and requires only a small amount of codein for his pain.

Case 2—Female, age thirty five years. Patient had far advanced disease of the buccal mucosa which was treated at another clinic. The treatment consisted of radium and electrocoagulation. She now has great pain over the distribution of the inferior dental nerve. Examination shows the malignancy to be apparently under control. There is a small area of necrosis in the alveolar border of the right lower jaw due to radium. From the x ray picture it would appear to be a radium necrosis. We injected the third division with 90 per cent alcohol. This produced anesthesia of one half of the tongue, the buccal surface, and of the area of the necrosis. The pain has apparently disappeared. We removed a large amount of the necrosed bone without any additional anesthesia. Patient has gained in weight and is eating and sleeping well.

Case 3—This patient has a malignancy involving the upper jaw and lip. The disease has recurred and the case is hopeless. The patient could not sleep or eat. Large amounts of morphin gave relief only for a short time. The pain extended over the lower two branches of the fifth nerve. As his physical condition was poor we injected the Gasserian ganglion with 90 per cent

alcohol and obtained anesthesia of the entire side of the face
This gave prompt relief from pain

The injection is given by introducing a needle through the cheek to the base of the skull and then through the foramen ovale. About $\frac{1}{2}$ c c of alcohol is injected. It is very gratifying to be able to relieve these individuals of the excruciating pain from which they suffer. As anesthesia is produced in most cases of the entire distribution of the fifth nerve, one must be careful to prevent injury to the eye. So far I have never lost an eye after an injection.

The next patient has pain in the second and third division of the fifth nerve and I am going to inject the ganglion, following the method of Hartel. The needle is introduced at a distance of 2 c c from the angle of the mouth the tip of the needle is now entering the foramen. The alcohol is injected slowly. I am now using novocain as a test. Note the dilatation of the pupil and the blushing of the affected side of the face. The patient now has anesthesia to the pin prick of the affected side. This will occur as soon as the sensory nerve is hit.

When the pain is in the anterior two thirds of the tongue or in the area of the fifth nerve injections are satisfactory. As these patients are hypersensitive to pain we give a few whiffs of chloroform.

Frequently it is impossible in malignancies of the upper jaw to afford the patient this type of relief. We then resect the Gasserian ganglion under local anesthesia. This is illustrated in the following case.

A colored woman with malignancy of the floor of the mouth and buccal mucosa. Large doses of morphin gave but temporary relief. Now you will note she has loss of sensation over the lower two branches. This operation is very satisfactory where the condition of the patient permits its use.

The next case is one of malignancy of the posterior third of the tongue. This patient suffered great pain. This area is supplied by the ninth and deep cervical branch from the cervical plexus. What can be done for him? It is possible where the glands are not too extensive to dissect the carotid sheath and

pull on the cranial nerves and cut or pull over the cranial nerves and on the cervical nerves. The will of the nerve. We have a small amount to have the cranial nerves divided intracranially. However the 2nd cranial nerve. We will have some of the procedures for the 2nd cranial nerve and the 3rd cranial nerves.

1. Alcohol. Injection into the third division and 2nd division the second division of the cranial nerve 2. It leaves the skull. If for any reason it is not possible to inject alcohol 1, then 2. The injection of the ganglion can be performed. Resection of the sensory root of the ganglion is preferable where the physical condition permits.

For pain in the distribution of the cranial nerve, cranial resection of this nerve when possible should be performed and when not we should do an intracranial resection.

For pain in the neck we should resect the cervical branches of the cervical plexus.

A combination of one or more of these procedures is frequently required.

and 3 mm in length. It is employed for implantation into and about malignant lesions of a more or less localized nature and in areas where it is difficult to use filtered applicators. Within the past month G. Failla, Physicist to the Memorial Hospital, New York City, has perfected a method of using a gold tube in place of the glass. This improvement of the bare tube possesses the distinct advantage of eliminating the very soft beta radiation which sets up a rather severe reaction in the tissues. The bare tube is inserted into the growth by means of a hollow steel needle 20 cm in length and 3 to 4 mm in diameter (Fig. 142). After boiling the bare tubes in special aluminum containers for three minutes along with the steel needle, the radon tube is inserted into the lumen of the needle placed in the tissues and ejected by means of a plunger which extends a minute distance beyond the end of the needle. The steel needles require considerable care, as a little rust within the barrel will cause the plunger to jam or band. When not in use they are kept in oil and are sterilized in boiling water before operations. Upon completion of the operation the needle is cleaned with water, alcohol and ether, and then placed in oil until used again.

The advantages of implantation of the bare tube of radon over the larger needle containing the element are many, chief of which are the ease of application and less trauma. No complaint has ever been made due to the tube producing foreign body reaction. They lend themselves very admirably in the radiation of small recurrent lymph nodes in the cervical and axillary regions, in the skin recurrences of mammary cancer, and in intra-oral lesions and their neck metastases. Their employment in gynecologic conditions is discussed elsewhere in this volume. The use of tubes of too great strength will cause a severe reaction with attendant sloughing and frequently produce much pain and discomfort to the patient. We have found that tubes of five tenths to seven tenths of a millicurie in strength produce the best therapeutic effect associated with the least discomfort to the patient. Bare tubes containing 1 millicurie or more should rarely, if ever, be used as they will cause undue sloughing and severe pain.

The larger size of glass tubes are about 14 mm in length and 2 mm in diameter. They average about 200 to 250 millicuries in strength the day they are collected and are always used with filtration. The Physical Department encloses them in a silver capsule the walls of which are $\frac{1}{2}$ mm in thickness. As no two tubes contain identical amounts of emanation the silver tubes have been enameled in different color combinations so that they may be easily identified. Occasionally it is necessary to employ a lighter filter than silver, at such times we use aluminum capsules 1 mm in thickness. The silver filtered tubes therefore, form the basis for 98 per cent of our filtered applications. They permit about 10 per cent of the total beta radiation to pass through for therapeutic use and serve as a source of the gamma rays used in deep treatments.

Small superficial epitheliomata of the skin senile keratoses and like lesions are easily treated by direct silver tube application. They are applied in contact with the lesion by means of adhesive strips, as a rule we use one tube to a square centimeter of tissue. The dosage which is destructive, averages fifty to sixty millicurie hours per tube used. The erythema dosage when using a silver filter at contact of 1 mm in thickness is about twenty two millicurie hours. In removing verruca and other such benign lesions a dosage of thirty five millicurie hours is about the right for the average wart. The uninvolved skin is protected by means of a lead strip a hole being reamed in the center of a piece of lead large enough to admit the wart. For small lesions occurring in the buccal mucosa and not too close to the alveoli two wooden tongue depressors are bound together at one end by a rubber band so as to produce a spring effect. At the opposite end the silver tubes are in direct contact with the lesion and the other blade serves as a clamp on the outside of the cheek adjacent to the silver tubes. Care should be taken that the applicator does not clamp too tightly.

In applying filtered emanation to surface lesions that are large or irregular a dental compound mold serves as an ideal container for the silver tubes. This compound is a paraffin

material employed by the dental profession in taking impressions for plates and bridges. The wax is placed in gauze and immersed in hot water for a few minutes to make it pliable. An exact mold of the lesion can then be made by working it in and around the growth. The wax is then allowed to harden, following which grooves are melted into it of sufficient size to hold the silver tubes (Fig 142). If several tubes are necessary they should

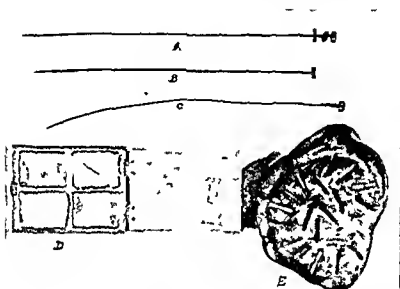


Fig 142—A Needle for implanting bare tubes $3\frac{1}{2}$ inches with plunger in place B needle C plunger D aluminum box used in sterilizing bare tubes Upper compartment shows four large glass tubes Lower left compartment shows three bare tubes E Dental compound mold Five silver tubes in place Other slots empty

all be approximately of the same strength. The same dosage is employed with this applicator as described above when applying radium by means of adhesive strips.

Several types of applicators have been devised by which gamma radiation alone may be used. They vary in size, shape, and the distance at which they are applied from the skin. The principle of filtration is identical in all. The silver tubes and brass

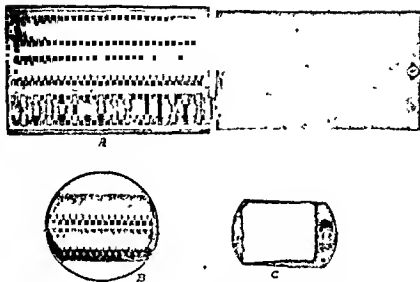


Fig 143 —A, Large rectangular brass tray, 7 cm by 10 cm One row of silver tubes in place, B, small circular brass tray, C, lid to B showing strength of radon available on date indicated

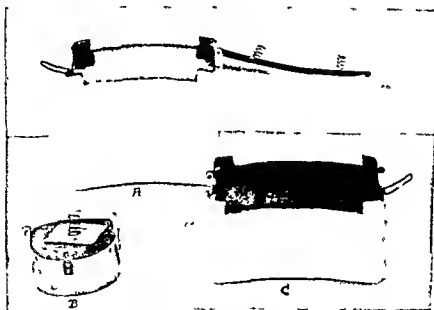


FIG. 144 — A, Ten cm distance box, B, 3 cm distance box, C, 6 cm distance box. With tray in place, a radium pack

container suffice to eliminate all but the hard gamma radiation. We use three different sized radium packs, the smaller has a round tray of brass with a rectangular receptacle for the placement of the silver tubes the area of which is 24 sq cm. This pack is used for relatively superficial metastatic nodes of small size at a distance of 3 cm from the skin. The dose that will produce a mild erythema is approximately twenty two hundred millicurie hours, and three thousand millicurie hours is the absolute limit of the skin tolerance.

A larger rectangular tray also of brass, covers an area of 70 sq cm and contains slots for three rows of silver tubes



Fig 145 —A Cervical tube with silk cord and strength of radon shown on dependent end. This tube contains B Brass capsule (closed) C, silver tube D, brass capsule (open)

(Fig 143) It is used for deep seated growths and metastases or in superficial lesions primary and secondary, the area of which is too large for the smaller pack to cover. The larger tray is used 6, 10 and 15 cm from the skin, depending upon the depth, location, and amount of gamma radiation the tumor requires. At 6 cm the limit of dosage is twelve thousand millicurie hours at 10 cm it is twenty two thousand, and at 15 cm forty thousand millicurie hours is the limit.

Box like frames constructed of bass wood and closed at both ends by mica are used to support the brass trays. These boxes are either strapped to the patient by adhesive or applied by

means of a bandage, following which the tray of radium is fastened on the box and held in place with a spring-like clamp and latched (Fig. 144). Any portion of the patient's body which is in greater proximity to the brass tray than the area being treated must be protected by a lead shield. The bottoms of the boxes, *i. e.*, the surfaces coming in contact with the skin, are



Fig. 146 —Patient receiving a radium pack to stent for carcinoma of the tonsil. Note lead shoulder protector.

concave, the arc of which is part of a circle 80 cm. in diameter. The tops of the boxes are parallel to this and the tray curves in a corresponding manner.

For the radiation of body tubes and cavities, such as the rectum, cervix, esophagus, etc., an interlocking brass capsule is used (Fig. 145). This capsule is 2 cm. long and 8 mm i

ter with a wall 1 mm in thickness. It will hold one silver tube. The brass capsule is always covered by a piece of rubber tubing which will absorb the secondary radiation.

Special applicators are often constructed to fit in special situations where the ordinary appliances are unsuitable. We are indebted to G. Failla, Physicist to the Memorial Hospital, for the majority of the applicators in use at our clinic.

CLINIC OF DR J DOUGLAS MORGAN

RADIOLOGICAL DEPARTMENT, PHILADELPHIA GENERAL HOSPITAL

THE ELECTROTHERMIC METHODS IN THE TREATMENT OF MALIGNANT DISEASES

THE electrothermic methods depend for their results on the high frequency currents

A high frequency current is one that periodically reverses the direction of its flow at an exceedingly high rate. It may be produced as follows: the outer coatings of two Leyden jars are connected by a coil of wire (solenoid); the inner coatings terminate in knobs whose distance apart can be regulated. The jars can be charged from a static machine, from an induction coil, or through a step-up transformer from the alternating current supply mains. When the circuit is closed the inner coats of the jars become charged, one positively, the other negatively. Charges of opposite sign are induced on the outer coats. As the jars become fully charged they overflow, and a torrent of sparks darts across the spark gap. The charges on the inner coats thus neutralize one another, and simultaneously the induced charges on the outer coats neutralize one another, and a momentary current passes along the solenoid. Each spark appears to be single, but in reality consists of a series of sparks, each one being smaller than the one which preceded it, until the charges on each side of the jar being neutralized, the sparking comes to an end. The rate at which the Leyden jars are charged is perhaps a few thousand times a minute, whereas the oscillations in each discharge may number some millions per second.

Such a current is, strictly speaking, an interrupted high frequency current (Fig. 148), the alternations are caused by the condenser (Leyden jar) discharge (sparking) and the inter

ruptions by the time it takes for the condensers to become fully charged, and to overflow. As a comparison of the time taken

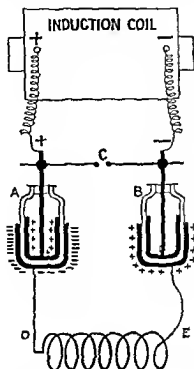


Fig 147 —(From Morgan *Electrothermic Methods in Neoplastic Diseases*, published by F A Davis Company)

up by the alternations with that occupied by the intervals we may when using certain factors represent the oscillations for four waves (a to b) as 1 inch in which case with the same factors

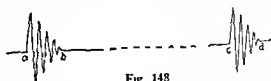


Fig 148

the intervals between oscillations (b to c) would be represented by 18 000 feet (Jenks and Clarke). Yet so rapid are the discharges that the current seems to be continuous.

A true continuous high frequency current can only be obtained by using an audion tube. The undamped oscillations of such a current are all of equal amplitude.

The high frequency current that is to be used on the patient is not taken from the solenoid directly but from a secondary coil placed in close proximity to it. This coil is made up of only one layer of wire whose turns are well separated, and receive high frequency oscillations by induction.

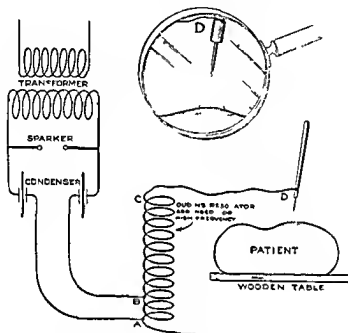


Fig 149 —(From Morgan Electrothermic Methods in Neoplastic Diseases published by F. A. Davis Company.)

Oudin in 1892 found that by causing the high frequency from the condenser to pass through a number of helices of copper wire the number of loops in the primary circuit being properly proportioned he obtained, in the continuation of these loops resonance effects, that is when the periods of oscillation due to inductance capacity, and resistance were balanced he obtained from the free end of the remaining helices of his resonator a high frequency current of enormously increased voltage vibrating in sympathy with the high frequency lower potential current of the first few loops. This is a monopolar current, so

known as the Oudin current. The bipolar or d'Arsonval current is obtained from the extremities of the secondary high frequency coil. Multiple spark gaps are preferable to a single gap.

The current produced is of comparatively lower voltage but of higher amperage than the monopolar current (Fig 150). When the electrodes carrying even moderately strong galvanic or faradic currents are applied to the body painful contractions or prolonged spasms of the muscles are produced and there is a stimulation of the sensitive tissues producing subjective sensations such as burning pains etc.

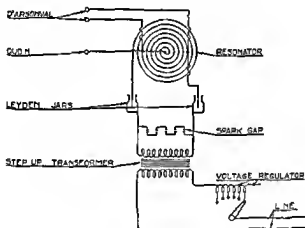


Fig 150 —(From Morgan Electrothermic Methods in Neoplastic Diseases published by F. A. Davis Company)

These sensations are supposed to be due to the movement of ions through the sensory nerves and end organs. If the current flows constantly in one direction and with unvarying strength the muscles remain unaffected in other words the regular flow of ions may stimulate sensory nerves but not motor nerves or voluntary muscles. If the current is cut off however, and the flow of ions brought to a sudden stop the muscles will give a single twitch which may be painful. This will be repeated when the current is once more switched on. A sudden reversal of direction of the ions will produce similar results. When the

reversal is slow no contraction of the muscles will occur but a sensation of pricking will be noticed due to the stimulation of the sensory nerves. When the reversals are sudden and of sufficient frequency (faradic) muscular contractions and painful spasms will result. Finally when the frequency of reversal becomes extremely high (high frequency) there will be no sensory or muscular response as the ions which have mass and therefore inertia are unable to respond sufficiently rapidly. This accounts for the fact that the muscles and the body in general do not perceive any shock even when comparatively large high frequency currents are used.

When a current flows through a conductor (whether a wire or the body tissues) energy is absorbed in overcoming the resistance and the conductor becomes heated. When using a galvanic or faradic current of a strength commensurate with safety and comfort the heating effect is inappreciable but it becomes evident when using the larger currents of high frequency which are permissible on the basis of what was said in the preceding paragraph. The rising of the temperature of the tissues lying between the electrodes of a high frequency current is known as diathermy because the heat passes through the depths of the tissues or as endothermy because it is generated within the tissues and does not come from without. It is an example of a physical effect (thermal) as opposed to the chemical or physicochemical (ionic) effect of the constant current and the currents of low frequency.

It is probable that the action of the high frequency currents upon the patients is chiefly a result of this liberation of heat in the tissues. There is a general rise of body temperature which is due to the heating not only of the fixed tissues but also of the circulating blood. Accompanying this general effect there is a quickening of the cardiac action and more or less sweating. Respiration is affected in that both the intake of oxygen and the output of carbon dioxide are lessened. The general blood pressure is lowered. Venous congestion when present is relieved.

The term medical diathermy includes these and all other of the physiologic effects of the high frequency current.

Surgical diathermy on the other hand is used to designate the methods of employing these currents to produce cell destruction Wyeth of New York has suggested the term endothermy¹ for these latter methods limiting diathermy to those producing physiologic effects In this sense it will be used on the present occasion It is intended that endothermy meaning heat within shall distinctly differentiate these methods from all others employing surface application of heat such as the actual cautery the electrocautery the Paquelin cautery fulguration etc None of these has anything to do with endothermy for in none of them is the heat (on which each depends for its results) generated in the tissues themselves which is of course the essential factor in endothermy In using any form of cautery the latter is raised to a dull red or even a bright red heat and applied to the surface of the tissue to be destroyed The surface cells are at once cauterized and a hard dry scab

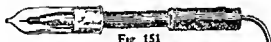


Fig 151

formed which prevents the further penetration of the heat The effect is very superficial as compared with the heat penetration of endothermy Also following so much cell destruction there results a scar which contains much fibrous tissue and keloid is a frequent sequence where the skin has been involved

Even fulguration although the product of the high frequency current is only another form of applying surface heat

As originally described by Pozzi² in 1907 it requires the directing upon the tissues of sparks of high frequency and high tension given off by a metal electrode of small diameter either bare or surrounded by an isolating cylinder which is connected with the end terminal of an Oudin resonator (Figs 149 151) While the method is of value in certain superficial conditions the sparks have no destructive effect beyond a depth of a few millimeters and are therefore insufficient when destroying a neoplasm of any considerable size

¹ Previously employed by Delbourn and Laquerre

² Revere claims to have used this method in 1900

There are two methods of applying endothermy, namely, electrodesiccation and electrocoagulation

Electrodesiccation, originated by Dr W L Clark, of Philadelphia, consists in the use of a monopolar (Oudin) current of moderate strength applied by means of a sharp needle-electrode (Fig 152) The point of the needle is placed in contact with the surface of the tissue to be destroyed, or inserted to whatever depth is required The resulting effect will depend on the strength of the current used the depth to which the needle is inserted, and the length of time of the application The result is the production in the tissues themselves (the needle always remains cold) of just sufficient heat to drive off the water in the tissue cells Histologically, a section of tissue so treated shows the cells to be shrunken and shriveled and their nuclei

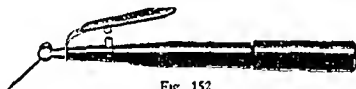


Fig 152

condensed and elongated with a suggestion of cell outline the whole assuming a mummified appearance (Asnis)

Since, by the desiccation method, the mode of cell death is associated with very little degenerative change and scant disintegrated material, there is but a small amount of fibrous tissue as an end result This method is therefore used advantageously when the lesion is localized and when good cosmetic results are essential, as, for example, in removing skin blemishes, precancerous dermatoses, minor gynecologic conditions, such as cervical erosions or urethral caruncles, eye conditions, such as corneal ulcers, chalazion and trichoma, where the subsequent formation of scar tissue would be most undesirable, or neoplasms of the vocal cords, where impairment of function must be avoided Desiccation is also of value in epulis and of carcinoma of the lip alveolar process, or tonsil Nor is there any surgical procedure that surpasses this method in the treatment of hemorrhoids

Electrodesiccation can in almost every case, be performed

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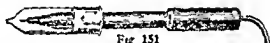


Fig 151

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¹ Previously employed by Delhew and Laquerr etc

² Reviere claims to have used this method in 1900

plates of bone being readily perforated, and larger masses so devitalized that they will sequestrate in from six to eight weeks.

When treating the soft tissues what is destroyed is, as a rule, immediately removed either by excision or curettage. The exposed base may then, when necessary, receive further treatment. When mucous surfaces are involved the destroyed tissue is, with few exceptions, allowed to separate slowly, owing to the greater danger of secondary hemorrhage in these localities.

When destroying a growth in close proximity to important blood-vessels it is advisable to ligate these before coagulating.

The main value of electrocoagulation lies in the success with which many malignant conditions, quite inoperable by the ordinary methods, may be treated. Malignant tissue may often be removed with more conservatism by electrocoagulation than with the knife. The neoplastic tissue is removed as a necrotic mass, the wound is completely sterilized, and the neighboring lymph- and blood-vessels are thrombosed, all of which are factors of importance as they tend to reduce the danger of metastasis. As operations by this method are practically bloodless, shock is reduced and secondary hemorrhage rare. Postoperative discomfort is reduced to a minimum and convalescence generally rapid.

The following are some of the conditions in which coagulation may be used with benefit: Carcinoma of the antrum may be destroyed by entering the latter through the hard palate, if this is involved; or through the cheek, either through the skin if this shows signs of malignancy, or through the anterior bony wall of the antrum after turning back a flap of the overlying healthy skin. If the eye is involved, the antrum may be entered through the floor of the orbit after exenteration, by electrocoagulation, of the eye.

When carcinoma of the tongue necessitates either partial or complete amputation it can be successfully performed by the coagulation method. Malignant tumors of the urinary bladder, also, may be destroyed by electrocoagulation, preferably through a suprapubic opening.

Diseased tonsils are sometimes destroyed by coagulation,

but, in reality, better results are obtained by desiccation, as the monopolar current produces quite sufficient heat to cause dehydration with less actual cell destruction than occurs with the bipolar current, and consequently, with a corresponding freedom from subsequent scar formation. This operation can be done under local anesthesia and the patient immediately go about his business or pleasure with the minimum of postoperative discomfort.

More recently apparatus has been devised to supply undamped high frequency oscillations. These are obtained by introducing audion tubes into the circuit.

With such a current all the tissues, except bone, can be cut through with the needle-electrode as though with a sharp knife. Tissue disintegration occurs but is not due to heat, instead, it is said to be produced by the disruption of the molecules of protein and fat when a small arc is formed between the electrode and the tissues. This arc produces a very superficial coagulation, the result being that small capillaries are sealed with coagulated albuminoid substances which are later on readily absorbed in the blood stream. In consequence, the operation is attended with comparatively little capillary bleeding and with the minimum of shock.

Primary union readily occurs.

The electrode is held in the fingers much as one would a pen. With the proper regulation of the current it will have the effect of a fairy wand dividing the tissues almost before they are touched. Care must, therefore, be observed in its use as there is not the changing sense of resistance of the various tissues to which the surgeon is accustomed.

There are several disadvantages to the use of this current which should be mentioned. One is the cost of the necessary apparatus and the frailty of the audion tubes, another, the readiness with which the essential arc is choked out, and a third, the twitching (faradic effect) which occurs when muscle tissue is touched by the needle-electrode.

These disadvantages have been considerably overcome by a quite recent modification of the ordinary coagulation current.

which, though "damped" and "interrupted," has, by greatly reducing the time occupied by the interruptions, been transformed for practical purposes into a continuous high frequency current

With this, cutting is done by coagulation but this is found to be of such a superficial character (a fraction of a millimeter) that primary union of apposed surfaces readily takes place. Extensive operations, such as amputation of the breast and the removal of the axillary lymph glands, may be very successfully accomplished with this type of current

Indeed some surgeons are now giving this method the leading place and preference in their routine work, relegating the scalpel to a subordinate position

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x RAY DEPILATION IN TINEA TONSURANS¹

FREUND of Vienna in 1897 was the first to suggest the use of the x rays in the treatment of ringworm of the scalp. Sabouraud and Voire of France in 1904 employed a special radiometer and produced depilation with a single dose. Keimbock and later, Adamson suggested methods of dividing areas of the scalp for treatment. The treatment has since been simplified and given greater security through the introduction of the Coolidge tube, the interrupterless transformer and electrical methods of measuring dosage.

Ringworm of the scalp was in the pre Roentgen period a most difficult and refractory disease to treat particularly the microsporon type. Treated by the old methods of ointments and lotions the condition not infrequently lasted from one to two years. This was a serious matter for a child for tinea tonsurans is essentially a disease of school age and in many communities children were excluded from school during the contagious period of the disease.

Between 1917 and 1926 250 children were admitted for ringworm of the scalp in the Dermatologic Service of the Philadelphia General Hospital. These cases were treated by application of tincture of iodine ammoniated mercury or tar ointments hyper-tonic saline dressings vaccine therapy etc. Despite clipping the hair and the employment of the old approved methods infection frequently spread over the scalp. The average dura-

¹ This report is from the service of Dr Jay F Schramberg by his courtesy and with his valued assistance.

tion of treatment was ten months the longest period of residence on the hospital being twenty months. Children were thus debarred from the opportunities of school instruction during this period. Furthermore, as always occurs in institutions where children are kept together in groups, acute exanthematous disease not infrequently attacked the ringworm cases and ringworm was occasionally transmitted to other children. Apart from these disadvantages of long hospitalization there is always the economic cost to the institution. On account of these various causes and the prevalence of ringworm in Paris, that city some years ago instituted special ringworm schools for children suffering from tinea tonsurans. We believe these have been rendered unnecessary by the improved methods of treatment.

Up to 1925 there was no x ray apparatus available for such accurate determination of dosage as is desirable and necessary in securing temporary depilation. The treatment of tinea tonsurans was then assigned to the Radiologic Clinic where modern apparatus was available. Previous attempts at depilation with a rather antiquated apparatus had led to unsatisfactory results in a few cases with permanent loss of hair.

The present routine treatment is as follows:

1. Upon admission the child has the hair clipped and the scalp washed with green soap and water until the crusts are removed. No ointments are applied.

2. The Kienbock-Adamson method of depilation is used. The head is measured. Starting 1 inch behind the hair line in the middle of the forehead, points 5 and 10 inches are marked off along the sagittal suture. Some slight adjustments of the anterior and posterior parts may be necessary in a very young patient.

3. From the 5 inch mark in the center of the calvarium a distance of 5 inches in the line of the coronal suture (right and left) is marked out. This should fall just above and anterior to the external ear. We now have five points which serve as the center for each of the five areas to be treated.

4. The head is so placed that the central ray is perpendicular to the tangents at each point. The factors for our particular

set up are 8 inches, spark gap 6 M A, 15 kv. transformer of 16 inches, and the time is three minutes, fifteen milliamperes, no filter. The ears, face, and neck are protected by $\frac{1}{8}$ inch lead plates.

Results—In two or three weeks the hair falls out. The depilation is complete leaving the child's head with a single hair. The areas infected by the tinea can be readily distinguished as they present a fine whitish desquamation.

We have now treated 34 cases in this manner. There has been no permanent alopecia. The hair has grown again in three months with no appreciable change. There have been no readmissions for reinfection. Cross infections are rare. These children are only in the hospital a month. When the hair has completely disappeared, the head is washed again with green soap and rinsed in 1:10,000 bichlorid of mercury.

The x-ray treatment of ringworm of the scalp and of that rebellious disease, favus, is today recognized as the treatment par excellence. It has the advantages of sureness and rapidity of result. It is safe when carried out by an expert, but should not be attempted by those with inadequate skill or knowledge. The hair fall should result from a single exposure. Repeated treatment may lead to permanent hair loss. Nothing more than a slight redness should be induced and in many cases even this does not occur. The factors of time of exposure, distance, spark gap, and amperage must be accurately adjusted. The formula for each apparatus must be worked out.

The purpose of this brief report is to emphasize the importance of the newer methods over the old, particularly from the economic standpoint.

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ROENTGENOTHERAPY IN DISORDERS OF THE RESPIRATORY TRACT, PARTICULARLY THOSE ASSOCIATED WITH ENLARGEMENT OR PERSISTENCE OF THE THYMUS GLAND, AND THOSE ASSOCIATED WITH UNRESOLVED PNEUMONIC EXUDATES

ENLARGED or persistent thymus gland is sometimes found in routine x ray examination of the chest in infants and children. It would be found more frequently if suspected oftener in patients showing respiratory disorder. Articles on this subject in medical literature are increasing in number and stress is laid upon the frequency of occurrence of a dangerous degree of thymic enlargement in infants. Moore,¹ who was formerly an intern in this Hospital writing on this subject recently gave a good account of the clinical findings. He states that he finds evidence of enlarged thymus in infants with great frequency and considers it a common not a rare condition but one which is commonly ignored or misinterpreted. The patient may present few symptoms or have many alarming attacks but only a small percentage die as a result of this condition. In his experience symptoms of obstructed breathing and croupy cough have been the exception and not the rule. The most common symptoms are transient cyanosis with shallow respiration and marked prostration. Cyanotic attacks in an apparently well baby with normal temperature are nearly always due to enlarged thymus. Severe convulsions without fever or other apparent causes are frequently due to enlarged thymus. Breath holding in children of the runabout age followed by unconsciousness as a result of temper or a trivial injury invariably proves to be the result of enlarged thymus. Any infant with persistent noisy breathing

or marked choking symptoms occurring with the slightest cold should be suspected. Moore mentions the occurrence of a family tendency to thymic enlargement and cites two instances. In one family 4 babies and in another 5 died suddenly, apparently as the result of enlarged thymus.

It is important to note symptoms pointing to thymic enlargement in infants as sudden death in infancy and early childhood is a not infrequent occurrence, and the treatment of this condition is simple, relatively safe, and usually satisfactory. In older children it is well to think of thymic enlargement in patients showing obstructed breathing with adenoids, particularly adenoids recurring after previous operation for their removal, hypertrophic tonsillar tissue and redundant lymphoid tissue deposits on the posterior pharyngeal wall and at the base of the tongue. A tendency to asthmatic attacks and frequent colds with the appearance of lymphoid hyperplasia in the fauces and pharynx is suspicious, and choking or breathlessness on excitement should be looked upon with serious suspicion. We have noted symptoms of substernal pressure in adults, coming on with great suddenness and sufficiently severe to be alarming which cleared up after radiation of the thymus region. While the x ray examination was doubtful in its result, associated findings caused a strong suspicion to be attached to the thymus in these cases and the result of treatment tended to confirm the view that the thymus was concerned in these attacks.

The thymus tissue is particularly susceptible to radiation therapy and abnormal enlargements of this gland yield readily to mild treatment with a reduction in size as shown by physical examinations and Roentgen plates, and with a satisfactory clearing up not only of symptoms but also, at times, of the associated abnormal deposits of redundant lymphoid tissue.

The thymus is a gland regarding the functions of which our knowledge is limited, although there has been an immense amount of speculation on this question. It is derived from epithelial tissue, is well developed in fetal life the epithelial elements forming a gland like structure and becoming densely filled with lymphoid cells. Whorls of cells form the so called corpuscles of

Hassel which are a characteristic of the thymus gland. There has been considerable discussion as to whether the lymphoid cells of the thymus gland are true lymphocytes or cells of a specialized type. It is claimed by some observers that the thymus lymphoid cells show distinctive differences in their chemical composition from the lymphocytes of other portions of the body. In the human being the weight of the gland in comparison to the body weight is at about its maximum at birth, but its actual weight normally shows increase thereafter up to about the time of puberty, decreasing after that time. Hammar gives the average weight in infants at 12 grams and at puberty 25 grams. There is a rather rapid reduction in the size and cellular elements of the thymus during later life, and of the structure remaining much is made up of fat and connective tissue.

Study of the functions of this gland has been carried on by experimental removal of the gland in animals, feeding of gland substance, observation of case of known gland abnormalities, and experiments dealing with the relation of the thymus to other glands. Conclusions drawn from experimental removal of the glands are contradictory on many points, but certain observations seem to be fairly established. Total removal of the thymus in very young animals exerts an influence on growth and development, it influences the development of the testes. Castration delays the involution of the thymus. Feeding of the thymus tissue to tadpoles was shown by Gudernatsch to increase their growth, but to delay their maturation in contradistinction to the effect of feeding thyroid substance, which hastened maturation but checked growth. Marine, Manley, and Bauman⁴ state that thyroidectomy hastens, and gonadectomy delays, thymic involution. Suprarenalectomy delays involution and may even cause regeneration of lymphoid tissues. Thyroidectomy prevents this reaction. A syndrome can be produced experimentally by suprarenalectomy and gonadectomy which resembles status thymicolymphaticus. D. Noel Paton,³ who has contributed much to the study of the thymus gland in the past, has recently reviewed this subject. He cites the work of Marine and his associates and concludes that their experiments confirm his

observations that before puberty the thymus exercises an influence on the growth of the body which influence wanes as the testes develop and the thymus atrophies but which may be maintained after castration. Usually the action of the two glands is a balanced one but after removal of one influence the increased functional activity of the other may establish compensation. Giordano⁴ on the basis of a large number of observed cases of thyroid disease states that persistent thymus is usual in toxic and not present in non toxic goiter cases.

The thymus substance is rich in nuclear material and phosphorus compounds particularly lecithin and some of the effects ascribed to a specific secretion may be purely chemical in their mode of action. Sajous⁵ urged the view years ago that a chief function of the thymus was as a reservoir for phosphorus compounds to be supplied as needed by various body tissues.

The mechanism of the so-called thymic death is not understood. It has been held that the usual cause of death is pressure on the trachea by a suddenly congested and engorged thymus gland. It is well known that the gland is subject to sudden increase in bulk and density assumed to be caused by congestion this tendency to enlargement under strain or excitement is taken advantage of by the roentgenologist in making an examination for enlarged thymus in a child by exposing the plate after the child has cried or struggled. The gland at this time will appear larger and denser than when the child is resting quietly. Lateral views of the chest in thymic cases may show distinct compression of the trachea by the enlarged gland. The gland is situated at a very constricted position of the thorax and an enlarged gland can crowd the trachea to a serious degree particularly when the head is thrown back with full extension of the neck. On the other hand Paton states that it is difficult to decide whether the large thymus found in many big flabby babies and which by some is considered to be correlated with the condition described

these cases with another infant showing a blood-sugar determination of 25 mg. who had an acute suprarenal hemorrhage, they advance the hypothesis that death in status thymicolymphaticus may be due to an acute suprarenal insufficiency.

Symmers⁷ considers the question of status thymicolymphaticus very fully on the basis of 249 postmortem examinations. He gives credit to C. Norris, Pathologist at Bellevue Hospital, for the recognition of this syndrome. His cases were largely among adults and the recognition of this condition was based on structural peculiarities of bodily development and necrotic areas in the lymphoid structures and in the thymus. A large proportion of his cases were of what he called the recessive stage. The thymus had undergone atrophy, but structural developmental faults, particularly hypoplasia of the arterial system, tended to render these individuals defective physically; they were peculiarly subject to acute infections, and their histories showed them to be abnormal nervously or mentally.

The danger of sudden death in an infant with a markedly enlarged thymus is one that should be recognized. This danger can probably be largely avoided by radiation of the gland. How far this treatment goes in modifying other features of the child's development and preventing the picture of adult thymicolymphatism is not clear, but the general impression that the effect of treatment on general condition and development is good seems to be warranted. Radiotherapy as practised is not comparable to experimental thymectomy. Involution of the enlarged gland is extremely rapid after treatment, but regeneration takes place. There have been reports of death following treatment in desperate cases, and there may be an immediate reaction with increases of symptoms during the first twenty-four hours following the treatment, but any untoward results are unusual and this method of treatment may be rated as a conservation and a safe measure for relief from the symptoms of obstructed breathing in infants. In individuals showing enlarged thymus gland anesthesia and operation are rightly considered to be attended with undue risk. If radiation of the gland area with the reduction of the size of the gland is accomplished the risk of such

sternum normal heart and lungs Symptoms had persisted about two years Report of x ray of the thymus was doubtful as regards enlarged or persistent gland She was treated by Dr Bromer She reports very marked improvement in her general nervous condition and an absence since treatment of the suffocative attacks which formerly terrified her She eats what she pleases and swallows easily Tonsillectomy advised

Case 4 —In the summer of 1925 a baby girl aged one year was seen on account of coughing spells and nasal obstruction She showed enlarged tonsils and severe adenoid obstruction of the post nasal space The mother suffered from whooping cough at the time of this child's birth and the child for some weeks after birth was subject to frequent paroxysms of coughing and choking which resembled whooping cough These attacks diminished in frequency but after a year there was some respiratory trouble remaining Tonsillectomy was advised No thymus dulness was apparent but it was thought prudent to x ray the chest before operation x Ray by Drs Pfahler and Widman showed a large and dense thymus gland Treatment by x ray was followed by prompt improvement in symptoms and nasal breathing became free One year later she was again examined by x ray Enlargement of the gland was still present and there was still slight tendency to catching the breath and crowing when crying or struggling Further treatment was given Owing to the improvement in symptoms operation was deferred in this case

Case 5 —A girl of eight years had tonsils and adenoids removed by an eminent laryngologist less than a year before this consultation There has continued a tendency to frequent colds nasal obstruction and adenoid appearance Examination of the nose by the previous operator records abundant adenoid tissue blocking the nasopharynx There is a troublesome twitching of the muscles about one eye An error of refraction was corrected by glasses with little effect in the twitching An x ray of the thymus showed a large gland This was treated Since treatment of the gland there has been a marked diminution of the

adenoids and recently a disappearance of the muscle twitching. Child also had thyroid substance given over a considerable time.

Case 6.—A girl of thirteen years of age was seen in July. She has had attacks of asthma since taking cold last November; prior to that time was healthy. In January was told that she had asthma. Attacks come on four and five times a day and last about five minutes. She then gets relief and between attacks is free from symptoms. During these attacks her face becomes blue, she has to "holler for breath," and gets so short of breath that she thinks "her heart is going to burst." Seldom has any trouble at night. This girl is well developed and seems precocious physically and mentally, stands exceptionally well in school. The tonsils are in very bad condition. The chest shows poor expansion and small diaphragm excursion; probably some emphysema at this time. The heart sounds are good. There is increased dulness at the upper sternum which is suspicious of thymus enlargement. x-Ray examination indicated peribronchial and hilum thickening in each lung. Apices clear, enlarged mediastinal glands suspected. No apparent shadow of enlarged thymus. She received x-ray treatment of the thymus region with apparent benefit, the attacks ceasing. The tonsils were removed and there was prompt recovery from the operation.

Recent information is to the effect that after a period of good health there has been a return of respiratory trouble of some sort, and in spite of the seeming benefit for two or three months, this case is questionable and needs further observation.

Case 7.—A baby boy was admitted 3/20/24, at the age of nine months. Had double pneumonia; treated at another hospital; later sent to the mountains. Upon his return to the family attacks of suffocation when crying developed and were severe enough to frighten the family. He was suspected of thymus enlargement and sent here for treatment.

Three exposures were given by radium pack, one anterior and two posterior—3/20/24, 4/3/24, and 4/28/24: 6 cm. distance, four hours, six hours, and two hours, 5068, 3786, 1430 millicurie hours respectively.

In November 1925 the patient is a well developed normal child strong and active. No signs of endocrine disturbance no attacks since radiation.

Case 8 — Baby female aged three weeks. Shows symptoms of enlarged thymus since few days after birth. Treated September 1924 3555 millicurie hours 6 cm distance. Respiratory difficulty increased for twenty four hours following radiation. No trouble after leaving hospital.

Recent advices state that he has had no symptoms since treatment. This child's father is a physician and gives the history of the case as follows:

The youngster first showed symptoms on the day that he was three weeks old when he suddenly began crying and fretting and then took a long inspiration and simply ceased breathing. In this attack he probably stopped breathing for about ten seconds and became somewhat cyanotic but not alarmingly so. I believe he had two of these spells the first day. On the following day he continued having these attacks but each time he would become more cyanotic and the length of time between the attacks became shorter so that he must have had four in all the second day. On all occasions he would move around in his crib start to cry feebly and then suddenly take a long inspiration and cease breathing. After the first five or six of these spells it was necessary for us to give the child quite active artificial respiration and were it not for this fact I believe the child would have died. On the third day he began to have the attacks so frequently and became so cyanotic in each one that I called in Dr. John Scott of the Pediatric Staff of the University and he diagnosed the trouble as enlarged thymus and advised immediate x-ray to confirm his diagnosis. Dr. Pancoast saw the child in one of his attacks also and thought it unsafe to use any x-ray therapy where the room would have to be darkened. Dr. Bradley at the General Hospital gave the radium treatment as your records show. I kept him in touch with the after effects of the treatment. On the day that he had the treatment (the fourth day of the disease) I should judge that he had ten very

severe attacks of cyanosis, and apnea which are his chief symptoms. He had two spells during the time that he was being exposed to the radium rays. As I said before each attack was more severe than the preceding one and the most severe attack that he had probably lasted about two minutes although it seemed to be as many hours to us. That night the attacks began to fall off, both in severity and in the length of time between them. On the fifth day they had further let up and were quickly controlled. He must have had six mild attacks on this day. On the sixth day the symptoms left entirely and he had only two very mild attacks the entire day. From that time until the present he has had no signs of any trouble, and from all indications is a normal boy in every respect. In fact, he was a little ahead of the average in cutting teeth, sitting up, walking, talking, etc. The child has had the mumps, and several attacks of what I believe to be the 'hives,' generally caused from oranges or grapefruit, which I do not believe has anything to do with his enlarged thymus. With the exception of the six days that he had the thymus enlargement, I can say that he has been absolutely normal."

Case 9.—Baby, male aged two and a half years, admitted 5/28/26 for bronchitis. As an infant occasionally became blue and short of breath. Always had tendency to croupy cough. Wakes up at night wheezing, harsh breathing and croupy cough, has been in hospital twice with bronchitis and bronchopneumonia. Since June 19, 25 has had cough and wheezing almost continually except for remissions of only a few days' duration. At times the child becomes very blue. Examination shows the lungs well developed, considerable adiposity marked over hips, elbows, wrists, and ankles. Fontanels closed, but no signs of rickets. Tonsils enlarged and red, slight nasal discharge. High arched palate, slight thyroid fulness, chest shows rough breathing and prolonged expiration all over chest, occasional large rbronchi. There is dulness at mediastinum to level of second rib. The heart sounds are of good quality. a-Ray report indicates sella turcica of normal size. Impression, persistent thymus, endo-

may perhaps be materially helped by this means. It seems in some cases that the persistent exudate is strictly peribronchial the pulmonary structure being comparatively clear. These patients tend to show chronic bronchitis with asthmatic tendency or persistent asthma. They may respond well to radiation.

Riesman¹⁰ in 1922 reported cases of protracted unilateral bronchopneumonia of lobar distribution showing no breaking down of the lung structure or cavitation stating that these cases may drag on for years. Harkavy¹¹ wrote in 1922 on the rôle of unresolved pneumonia in bronchial asthma and discussed the question of irradiation of the lung areas in these cases. He reported several cases treated by x ray. These patients did not respond to cutaneous tests using the proteins of bacteria suspected in each case. The areas interpreted as unresolved pneumonia by x ray examinations could not be identified as such by physical examinations on account of the deep situation of the lesions and also on account of complicating emphysema. He had good results in some of his cases.

Bowditch and Leonard¹² have treated a large number of cases of whooping cough by x ray exposure with favorable results in some instances very strikingly so. As the paroxysms of cough persist for a long time after the sputum of the whooping cough patient is capable of transmitting the infection of it it is probable that the persistence of symptoms is due to peribronchial and peritracheal infiltration or exudate and it seems reasonable that the symptoms should be benefited by the x ray treatment.

Dr. Pancoast treated for me a patient who suffered from bronchitic asthma with advanced emphysema following a pneumonia of five years previous with very marked improvement. A boy who showed a patch of apparently unresolved or chronic pneumonia by x ray examination was examined after three years and this lesion was found to be unchanged. He had frequent colds and attacks of asthma. After x ray treatment physical signs and x ray evidence indicated that a prompt resolution of this area had occurred and his condition was markedly improved thereafter.

Tuberculosis should be ruled out by the most careful examina-

tions with repeated search of the sputum for tubercule bacilli, as there seems to be a feeling that a quiescent tuberculous focus in the lung may be awakened to activity by irradiation. It is needless to say that a Wassermann reaction should be performed in every case showing unresolved pulmonary exudate, as resolution is apt to be delayed in active or latent syphilis. In such cases resolution can be satisfactorily stimulated by antiluetic treatment by mercury and iodid. Parenthetically it may be remarked that the fact of such a lesion clearing up under treatment is no basis for considering it syphilis of the lung. Unresolved pulmonary exudates of pneumonic origin will clear up satisfactorily under x ray therapy and in response to iodid. Either of these measures must be employed with the greatest care if at all in the presence of tuberculosis.

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